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SCIENTIFIC PROCEEDINGS.

ABSTRACTS OF COMMUNICATIONS.

Sixty-first meeting.

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President Lusk in the chair.

1 (933)

The effect of potassium iodide, methylene blue and other substances applied to the embryo sacs of seed-plants.

By **D. T. MACDOUGAL.**

[*From the Desert Laboratory, Tucson, Arizona.*]

The results of some experiments at the New York Botanical Garden in 1905 showed that it was possible to introduce foreign substances into the ovaries of the higher plants, in such manner that the egg, or pollen-nuclei, were affected as to their genetic capacity.

Similar results were achieved independently four years later by Major Firth, of the British Royal Army Medical Corps, Dr. Firth being unaware of the previous discoveries.

The removal of my work to the Desert Laboratory in 1906 made it necessary to find new experimental material. Species suitable for the study of the modification of the germ-plasm by external agencies should be genetically simple, and preferably perennial, so that successive generations may be kept alive for comparison, and it is a great advantage if the plant can be brought to maturity in a single season.

Many-seeded ovaries, with the ovules standing in an open chamber, offer the best mechanical features, and naturally, only those which will recover from the traumatic effects of the necessary operations are of value to the experimenter. The above

conclusions are based upon a long series of failures of ovaries to mature upon cultures of treated species showing no departures, and upon progenies including notable departures, the parental forms of which proved to be a complex of elementary forms. Satisfactory conditions were finally obtained with a Scrophularia, native to the mountain tops of Arizona. Ovaries treated in 1911 with a solution of one part potassium iodide to 40,000 of distilled water, and the seedlings grown in 1912, included two individuals unlike the parental strain. These and their progeny are unlike their progenitors in the color-pattern of the flowers, the water-relations of the stems, the degree of differentiation of the tissues, the shape of the wings of the stems, the form and size of the flowers, the growth-correlations and venation of the leaves. The continuance of these features in the successive generations indicates a permanent modification of the germ-plasm.

Studies of the behavior of methylene blue, and other dyes, in the ovaries, show that, in some plants, introduced solutions may be taken up by the placenta and conducted through the funicular stalk to the antipodal region of the embryo-sac, finally staining the egg-cell.

In other cases, the cells of the micropylar opening are stained, and the pollen tube in passing through this might be affected, and might also take up free foreign solutions in the open cavity. It is evident, therefore, that in the introduction of substances into such an ovary, the effect would depend upon the simpler mechanical features of the operation, the stage of development of the separate ovules, the progress of the advancing pollen-tubes, and the varying dilution of the reagent in its diffusion through many membranes. The individuals resulting from a treatment, affecting one element only, would be of a hybrid nature: and might be if both were affected to an unlike degree, or in an unlike manner.

Duplication of effects is therefore not to be demanded as a test of such results and, if strict repetitions were obtained, the implication that premutations were present would be strong. The range of the departures is limited in expression by the morphological possibilities, but instead of being premutatory, may be considered to be the result of the direct action of the reagent

upon the colloidal complex of living matter. The compound used in obtaining the results described would have a neutralizing or coagulatory effect on protoplasm. Other reagents, facilitating hydratation, have been used on ovaries from which seeds have been obtained, the capacities of which are yet to be tested.

2 (934)

Studies on so-called protective ferments. II. Proteolytic enzyme is not specific.

By J. BRONFENBRENNER.

[*From the Pathological and Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pa.*]

If the serum of a pregnant woman is placed in a dialyzing thimble together with placenta in all respects as for an Abderhalden test, only at a temperature of 0° C., dialysis does not take place. Both the serum and placenta however undergo certain changes. Such a serum, when separated from the placenta and placed in the dialyzing thimble with fresh placenta, can no more induce any specific changes in placenta. And the placenta once placed in contact with a positive serum on ice and then separated from it, although it is not able to give up dialyzable substances by itself (if suspended in salt solution), acquires the property to do so in presence of any positive or negative, male or female fresh serum. The placenta was evidently "sensitized" and the serum exhausted of the specific substances present in pregnant serum. Moreover such a serum deprived of its specific properties still retains the ability of causing the appearance of dialyzable substances in presence of the sensitized placenta. Evidently we have here complete parallelism between this phenomenon and that of sensitization of erythrocytes by an active hemolytic serum.

In studying the complement activity of a pregnant individual's serum exhausted of its specific elements by the above method, it was found that the complement tends to deteriorate very rapidly, much more rapidly than in the male serum treated in an exactly

similar way. Parallel with the deterioration of the complement and in the inverse proportion, the amount of the dialyzable protein fraction increases. The analysis of this phenomenon which will be described in detail elsewhere, led to the conclusion that the serum of a pregnant woman, treated in the way described above, acquires the ability of digesting itself. Moreover any normal serum placed in contact with "sensitized" placenta acquires the same property, so that the Abderhalden reaction would seem to be composed of two phases: the one—specific—the sensitization of placenta; the other—non-specific—the autodigestion of the serum as a result of the presence of sensitized placenta. Thus the assumption of specific proteolytic ferments of Abderhalden becomes unnecessary.

3 (935)

Studies on so-called protective ferments. III. The Abderhalden reaction is not an adsorption phenomenon.

By J. BRONFENBRENNER.

[*From the Pathological and Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pa.*]

In the current literature attention has been directed by Plaut,[1] Kjergaard,[2] Herzfeld,[3] Peiper,[4] Flatow[5] and others to the fact that kaolin or starch as well as placenta protein if mixed in suitable proportions with any fresh serum is able to produce the appearance of dialyzable substances in the serum. There is no doubt that these experiments show that by the simple adsorption of inorganic substances as well as placenta, serum may be so changed as to give off dialyzable substances. The conclusion however of these authors that therefore the Abderhalden reaction is not specific was premature. For we know that for instance in immunity work, complement may be fixed or inactivated by many inorganic and almost any organic substances (this is why in

[1] Plaut, *Münch. med. Woch.*, 1914, No. 5, p. 238.

[2] Kjergaard, *Zeit. f. Imfz. Orig.*, XXII, No. 1, p. 31.

[3] Herzfeld, *Bioch. Zeitshr.*, 1914, I.

[4] Peiper, *D. Med. Woch.*, 1914, No. 29, p. 1467.

[5] Flatow, *Münch. med. Woch.*, 1914, No. 21, p. 1168.

preparing reagents for the final test it is essential to titrate them or to find a suitable dose which will not fix the complement by mere adsorption); but we do not doubt the specificity of the complement fixation in the Wassermann reaction for instance. Here the parallelism between the complement deviation test and the Abderhalden reaction is very striking and I shall in later publications endeavor to give the proof that this parallelism is not merely on the surface but fundamental. In my experience positive Abderhalden test is obtained invariably with sera of pregnant individuals, whereas non-pregnant women gave as a rule negative results, provided the amount of placenta used for the test was not excessive. Moreover the fact that the appearance of dialyzable substances can be invariably brought about in male serum by placenta, if the placenta was previously sensitized, led to the conclusion that it is the very union between the placenta and some part of the pregnant serum—which union is very similar to that of antigen and antibody—that brings about changes in the placenta which enable such placenta to cause the auto-digestion of any fresh serum.

As to the mechanism of such an action upon the serum, the explanation which suggests itself to me as the most probable is the following: the combination of antigen and antibody is accompanied by a physico-chemical change of the medium (such as is for instance recorded by the Meiostagmin reaction) which in turn causes the falling out or adsorption of some elements of the serum which originally prevented the action of the proteolytic enzymes normally present in any fresh serum. The same mechanism explains the auto-digestion of the serum in the case of kaolin and starch, only here the inhibiting substances are filtered out from the serum by simple adsorption as for instance is shown by Jobling and Petersen.[1]

[1] Jobling and Peterson, *Journ. of Exp. Med.*, 1914, XIX, p. 459.

4 (936)

Studies on so-called protective ferments. IV. The Abderhalden test is rendered negative by the addition of serum-antitrypsin.

By J. BRONFENBRENNER.

[*From the Pathological and Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pa.*]

The view which regards blood serum as a digestive fluid is not a new one, and the importance of the mechanism regulating the activity of the ferments of the blood while in the body has recently been clearly detailed by Dr. Victor C. Vaughan.[1] The study of these ferments was lately taken up by Jobling and Petersen[2] who showed that the non-saturated fatty acids of the serum are in a way responsible for the inactivity of the proteolytic enzymes in the blood.

The experiments have shown that—as I expected—serum extracted with chloroform gives up dialyzable substances reacting with Ninhydrin; I further ascertained that the addition of non-saturated fatty acids in form of soap or in form of large excess of normal serum reëstablished the antitryptic properties of the treated serum, thus stopping the appearance of dialyzable protein substances. I then tried to see if the same procedure would also stop the auto-digestion of the serum exposed to its own ferments through the action of kaolin or starch on the one hand, and of the antigen-antibody combination on the other. The experiments confirmed the expectations in every case completely, and I am therefore in a position to say that by the addition of the excess of whole normal serum as well as by the addition of saponified fatty acids of the serum, the Abderhalden reaction is invariably rendered negative, evidently through the arresting of the self-digestion of the serum.

The study of this question is not completed as yet, but even now it is possible to say that not only fatty acids, but also the serum-albumin tends to retard auto-digestion, while the addition

[1] *Jour. A. M. A.* 1914, Vol. 63, p. 365.

[2] *Jour. of Exp. Med.*, Vol, 19, 1914, p. 239.

of serum globulin seems to promote the appearance of dialyzable substances, probably on account of the digestion of the globulin by the serum ferment.

5 (937)

Studies on so-called protective ferments. V. The serum is the source of dialyzable substances.

By J. BRONFENBRENNER.

[*From the Pathological and Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pa.*]

In the experiments related above I have shown that the serum of a pregnant individual, placed in contact with placenta at 0° temperature and separated from the placenta by subsequent centrifugation, is capable of giving up dialyzable substances if placed in the incubator. Assuming that the cells of placenta were centrifuged down, the only explanation for the appearance of amino acids and polypeptids in such a serum was that the serum acquired the ability to digest itself. The fact that the addition of fresh placenta to such serum does not increase the degree of dialysis on the one hand, whereas on the other addition of serum globulin increases it very markedly—points toward the correctness of this assumption.

Some experiments conducted in my laboratory at present with placenta as well as with bacterial substrata will prove definitely that the substratum is not the source of dialyzable substances in the Abderhalden test. While these experiments are still in progress, I tried also to see if my assumption of the auto-digestion of serum in the Abderhalden test will hold good in the case of syphilis, for if the dialyzable substances should appear in this case, there will be no doubt as to their source, as the substratum in this case is not of protein nature.

As it was to be expected, the sera of syphilitics, when brought into dialyzing thimble with suitable amount of pure lipoid, often gave positive Abderhalden test, while sera of normal individuals, treated in similar way gave most often negative results. The adjustment of the amount of lipoid to be used in this test is very

important, as the excess of it may by simple adsorption cause non-specific reaction, just as in the Wassermann test, the improper dose of antigen may cause the fixation of the complement in normal cases. The number of experiments with this test is as yet too small to give a definite idea of its usefulness as compared with the Wassermann test for instance (and some of the results seem to show that the reaction can be missed even more easily than the Wassermann reaction in treated cases) but, what is important in connection with my previous work on the Abderhalden test, it shows that in the cases where this reaction is present it is the serum of the patient and not the substratum which offers the source of dialyzable substances.

6 (938)

The effect of the pituitary on the isolated human uterus. (Preliminary communication.)

By **C. C. LIEB.**

[*From the Pharmacological Laboratory, College of Physicians and Surgeons.*]

Kehrer claims that an extract of the posterior lobe of the pituitary gland is the ideal ecbolic. Indeed, he goes so far as to suggest that the secretion of this portion of the gland is the hormone which induces labor.

In studying the effects of pituitary extracts on isolated human Fallopian tubes and uteri my attention was arrested by the difference in the response of the non-pregnant and parturient organs. The contractions of the parturient tube and uterus were invariably increased in rate and strength when extracts of the gland were applied. The same stimulation was found when an ectopic tube was studied.

The effect of pituitary on the non-pregnant tube or uterus is wholly different. Small doses usually have no effect. Large doses, such as produce marked stimulation of the pregnant uterus, may cause a very definite depression or they may not influence the movements at all. To what is this change in the response of

the non-pregnant and parturient uterus due? The simplest explanation would be that, like the cat's uterus, the human organ changes its innervation, or, rather, during pregnancy its motor innervation becomes predominant. Such, however, is not the case, for epinephrine produces stimulation of the human uterus whether it is pregnant or not. Furthermore, the parturient uterus does not appear to be more susceptible to epinephrine. The only explanation which offers itself is that some substance sensitizes the uterus to pituitary. What this substance is, whether fetal or maternal in origin, I have not yet been able to determine. The sensitizer is certainly not epinephrine, because the previous application of this sympathonimetic amine does not influence in any way the reaction of the non-pregnant organ to pituitary. The difference in response of the two types of uteri throws some light on the discordant results which are said to follow its therapeutic use.

Quigley has made a very careful review of the clinical literature. From these reports and his own cases he concludes that pituitary extract is an efficient ecbolic only after labor has begun. Humpstone declares that pituitary will not induce labor and Hirsch has reported that it is of no value as an abortifacient. Patek claims that pituitary allays threatened abortion while Fischer urges that it be employed to complete a miscarriage.

These apparently divergent effects may be harmonized by assuming that the uterus must be sensitized before it will respond to the systemic administration of pituitary. During labor the uterus is so sensitized and hence its almost invariable stimulation. In earlier stages of pregnancy the uterus may be sensitized or not. If it is, pituitary will complete abortion or miscarriage. If it is not so sensitized, the administration is not followed by stimulation of the uterus. During threatened abortion a non-sensitized uterus may remain unaffected or it may be depressed. If it is depressed by pituitary the abortion is allayed. If the uterus is not affected the course of the miscarriage is not shortened.

How early may the uterus become sensitized to pituitary? The experiment on the tubal pregnancy indicates that six weeks after conception pituitary may have a stimulating effect. This also indicates quite clearly that unless we regard tubal rupture as

the result of true labor contractions, we can not assign to the posterior lobe of the hypophysis the rôle of hormone for the induction of normal labor. It is true that during pregnancy the pituitary gland hypertrophies and that after the expulsion of the fetus retrograde changes occur. This hypertrophy is limited to the true glandular lobes, the anterior and middle divisions. The posterior lobe shows no sign of increased activity. But it is from the posterior lobe, and from this alone, that the ecbolic principle can be obtained. Furthermore, Kohn denies the existence of an active substance in the posterior lobe during life. He believes that extracts of the gland owe their activity to some decomposition product which is formed during the manufacture of the extract. These facts seem to indicate that the posterior lobe is not concerned with normal labor. Though extracts of the posterior lobe are pharmacologically very active, the lobe itself is not essential to life. Complete removal of this portion of the gland does not interfere in any way with normal bodily activity. It is the anterior lobe which is essential to life. Oddly enough, extracts of this lobe have not been shown to have a demonstrable pharmacological activity. But it is this lobe which hypertrophies during pregnancy. It is apparent that if the pituitary gland is to be regarded as intimately concerned with the onset of labor, the hormone should be sought not in the posterior lobe but in the anterior portion of the gland.

7 (939)

On the action of temperature and humidity on the organism.

By FREDERIC S. LEE and ERNEST L. SCOTT.

[*From the Department of Physiology, Columbia University, New York.*]

The main object of the present research is to discover whether objective signs of physical inefficiency may be found in individuals when subjected to an atmosphere of high temperature and high humidity. Cats were used as the subject of experimentation, and were confined individually for a period of six hours within a small chamber supplied with abundant moving air. With one

group of animals the temperature averaged approximately 21° C. and the humidity approximately 54 per cent.; with the other a temperature of 33° C. and a humidity of 89 per cent. were employed; that is, the animals of the first group were kept under comfortable atmospheric conditions, those of the second group were given air approximating that of a hot, humid summer day. In some of the animals the rectal temperature was observed at the beginning and the end of the period of confinement. At the end of this period the cats were taken from the chamber and killed by instantaneous decapitation. The blood was collected for the estimation of sugar, and certain of the muscles were removed and stimulated until they were exhausted, each contraction being recorded graphically and the total duration of the working period and the total amount of work performed being determined. The average results of the observations on the muscles are presented herewith.

	Temperature in Degrees C.	Humidity in Per Cent.	Duration of Work in Minutes.	Work Done in Gm. Mm.	Percentage of Work Done.
Sternal strip of diaphragm...	21.3	55	196	157,665	100
	33	89	212	136,123	86
Extensor longus digitorum...	21	59	101	31,305	100
	32.6	89	80	25,714	82
Sartorius.....	21.7	49	138	46,598	100
	33	89	109	29,785	63.9

Under the influence of the high temperature and the high humidity, therefore, the total amount of work which the muscles are capable of doing before exhaustion sets in is markedly diminished; and the total period of working power is shortened, except in the case of the diaphragm.

The observations show that the bodily temperature of the animals rises in the atmosphere of high temperature and high humidity. This is seen from the following average temperatures.

Temperature of Air in Degrees C.	Humidity of Air in Per Cent.	Bodily Temperature before Confinement.	Bodily Temperature after Confinement.
21.4	50	39.13	39.03
33.1	89	39.33	39.81

In addition to any bearing which the content of sugar in the blood of these animals may have upon the problem in hand the apparatus offered a means for determining whether certain extreme weather conditions would introduce a disturbing factor in experiments involving the determination of sugar in the blood. In order to avoid vitiating the results by emotional hyperglycemia, only the blood from those animals which appeared quiet during confinement in the chamber and upon removal was taken for analysis. The normal or standard percentage of sugar in the blood of cats—0.069 per cent.—reported elsewhere by one of us,[1] was determined upon animals which could be presumed to be in every way comparable with those used in these experiments except for the experimental conditions. The results of our observations are as follows:

No. of Animals.	Temperature of Air in Degrees C.	Humidity of Air in Per Cent.	Sugar: Gm. Per Cent.		Sugar: Percentage of Standard	
			Actually Found.	Calculated to 30 Gms. of Blood per Kg. of Body Wt.	Actual.	Calculated.
9	21.27	56.44	0.068	0.067	98.6	94.8
5	33.08	89.50	0.060	0.057	87.0	83.0

It is thus seen that the average found for the cats kept at the low temperature and low humidity was practically identical with the standard, while the animals kept under the adverse conditions described gave an average of only 0.060 per cent., or 87 per cent. of the standard. The significance of this difference is somewhat difficult to determine; this is especially so in the absence of the coefficient of respiration. It is possible that less sugar is mobilized in response to the lessened heat requirements of the organism.

[1] E. L. Scott, *American Journal of Physiology*, 34, 1914, p. 271.

8 (940)

Studies of the basal metabolism and its relation to the body surface in obesity, myxedema, and pituitary disease.

By J. H. MEANS.[1]

[*From the Medical Service of the Mass. General Hospital.*]

The following determinations of basal metabolism were calculated by indirect calorimetry from the oxygen absorption and the R. Q., these factors being obtained by means of Benedict's unit apparatus (mouthpiece and spirometer). At least three ten-minute periods were run, and the average taken for that day's basal metabolism. In case I the calculation included the estimation of calories due to non-protein metabolism and to this was added that due to protein. In the other cases the protein metabolism was ignored. None of these cases had over 6–7 grams urinary nitrogen per day, so that the protein element would not affect the total calorie calculation by more than 1 to 2 per cent.

The body surface has been calculated by Meeh's formula and also by DuBois's.

The results are given in the table.

Cases studied were:

Case 1. Simple obesity of many years duration.

Case 2. Very marked obesity, also of many years duration.

Case 3. Sudden gain in weight in last year and a half. Sugar tolerance abnormally low. Thought to be hypopituitary. Said to have a polyuria, not noticed in ward.

Case 4. Acromegaly of long standing. Sugar tolerance now high. Thought to be going over into a hypopituitary stage.

Case 5. Typical myxedema. Never treated with thyroid.

Subject Dr. P. Normal control. Large muscular man.

In the cases studied the surface area by Meeh's formula was from 10 to 30 per cent. below that by DuBois's. In two cases of marked obesity the metabolism per square meter (DuBois) was

[1] Walcott Fellow in Clinical Medicine, Harvard University.

Subject.	Diagnosis.	Number of Basal Metabolism Determinations.	Height, Cms.	Weight, Kg.	Age.	Body Surface, Square Meters.		Calories per Kg. and 24 Hours.	Calories per Square Meter per Hour.		Percentage Variation from Normal (34.7 Cal. per S. M. + Hour).	
						Meeh.	DuBois.		Meeh.	DuBois.	Meeh.	Du Bois.
Case I, Mrs. McK..	Obesity	19	137	103 average	48	2.703	1.859	15.0	23.9	34.8	−31%	+ 0.3%
Case II, Mrs. B.....	Obesity	2	163	179	44	3.907	2.954	14.0	26.8	35.4	−23%	+ 2.0%
Case III, Mrs. M...	Obesity Hypo-pituitary?	2	161	87	28	2.419	2.009	17.2	26.0	31.1	−25%	−10.4%
Case IV, Mrs. C....	Acromegaly	1	160	80	65	2.280	2.060	19.3	28.2	31.2	−20%	−10.1%
Case V, Mrs. D.....	Myxedema	2	153	67	57	2.039	1.621	14.4	20.0	25.2	−42%	−27 %
Dr. P.....	Normal control	6	186	94	32	2.541	2.118	19.2	29.5	35.4	−15%	+ 2.0%

normal. One case of obesity thought to be of pituitary origin was 10 per cent. from the normal average and hence may be regarded as suspicious. The case of acromegaly was also 10 per cent. below, and the myxedema 27 per cent. below.

9 (941)

The energy metabolism of infants in relation to age and nutritive condition.

By JOHN R. MURLIN.

[*From the Physiological Laboratory of Cornell University Medical College, New York City.*]

Recent studies of the heat production of infants by Benedict and Talbot,[1] Bailey and Murlin[2] and Murlin and Hoobler[3] indicate a progressive increase from birth to the age of one year, whether the metabolism is reckoned on the basis of weight or on the basis of surface area (Meeh).

On the basis of weight the average metabolism of 13 newborn infants, determined while they were sleeping, is 1.87 calories per kilogram and hour; of normal infants between the ages of two and four months inclusive, it is 2.38 calories per kilogram and hour; between 6 and 12 months the average is 2.45 calories per kilogram and hour.

On the basis of a square meter of skin surface the metabolism of the newborns (up to 14 days of age) is, on the average, 25 calories per square meter and hour; of normal infants from two to four months inclusive, 35 calories per square meter and hour; and between six and twelve months the average is nearly 42 calories per square meter and hour. These differences on the basis of surface area are based on the assumption that the surface bears the same relation to weight ($11.9\sqrt[3]{(W)^2}$) in all.

An analysis of all the observations on infants between the ages of two months and one year studied by Howland,[4] Benedict

[1] Carnegie Institution of Washington, Publ. No. 201; also *Amer. Journ. Dis. of Children*, 1914, VIII, p. 1.

[2] *Proc.* of this Soc., 1914, XI, p. 109.

[3] *Ibid.*, 1914, XI, p. 115.

[4] *Zeitschr. f. physiolog. Chemie*, 1911, LXXIV, p. 1; also Trans. of XVth Cong. on Hygiene and Demography, 1912, II, Pt. II, p. 438.

and Talbot and Murlin and Hoobler shows that the normal, recently-fed, sleeping infant produces about two and a half calories per kilogram and hour. With but two exceptions (out of 48) the underweight and atrophic infants produce more than this and the overweight infants produce less. It is suggested, therefore, that for practical purposes two and one half calories per kilogram and hour or sixty (in round numbers) calories per kilogram and twenty-four hours may be regarded as the average normal heat production of sleeping infants within this range.

10 (942)

The measurement of the surface area of adults.

By **DELAFIELD DU BOIS** (by invitation) and **EUGENE F. DU BOIS.**

[*From the Russell Sage Institute of Pathology in affiliation with the Second Medical Division of Bellevue Hospital.*]

Meeh's[1] formula $K\ WT^{2/3}$ is accurate in principle only when applied to individuals of differing weights but of similar body form.

The surface area of five adults of widely different weights and forms was measured by the following method. The subject was dressed in a tight fitting suit of union underwear, the hands were covered with cotton gloves, the feet with socks and the head with a tight fitting bag of woven cotton material. The gloves were then covered with melted paraffin and over the rest of the surface strips of paper were pasted in such a manner that a stiff mould of the body was formed. This was then cut in small pieces which would lie flat. Patterns of these pieces were made by printing them on photographic paper of known area and weight. These patterns were then cut out and weighed and the surface areas of the various parts of body calculated.

Many linear measurements of the subject were taken and an effort made to find the length and average breadth of each part of the body. After numerous trials characteristic measurements of length and breadth were chosen. The products of the length and breadth when divided into the surface area as actually deter-

[1] Meeh, *Zeitschr. f. Biol.*, XV, 435.

mined, gave factors which varied but little in the five cases measured. The total surface area of the body can be estimated by multiplying the length, breadth and the proper constant for each part of the body and then adding the parts together. This new formula gave the following errors in the five cases measured: Small fat cretin +0.5 per cent.; short, stout man +1.3 per cent.; tall, thin man −3.8 per cent.; tall man of average build +0.9 per cent.; short, very fat woman +2.0 per cent.

Meeh's formula applied to these same individuals gave errors amounting to +21 per cent., +17 per cent., +7 per cent., +14 per cent. and +36 per cent. respectively. Bouchard[1] who measured a series of adults found the following errors in Meeh's formula: very thin woman −3 per cent., normal man +2 per cent., normal woman +14 per cent., large man +12 per cent., very fat man +33 per cent.

There seems to be a plus error in Meeh's formula which becomes very large in the case of fat individuals. Since Meeh's formula has been the standard for 35 years it is advisable for the present to retain it in the case of individuals who are thin or of approximately the normal build, since, in their case, the error is not great. In the case of fat people or those of unusual body shape it is preferable to make use of the proposed formula which is determined by linear measurement alone.

CONSTANTS AND MEASUREMENTS USED IN FORMULA.

Head, AB, 0.308.
A, around vertex and chin.
B, around occiput and forehead, just above eyebrows.
Arms, $F(G + H + I)$, 0.558.
F, outer end of clavicle to lower border of radius.
G, circumference of arm at level of upper border of axilla.
H, largest circumference of forearm.
I, smallest circumference of wrist.
Hands, JK, 2.22.
J, lower posterior border of radius to tip of second finger.
K, circumference of open hand at knuckles.
Trunk, $L(M + N)$, 0.703.

[1] Bouchard, "Traite de Pathologie generale," Paris, 1900, III, 200, 384.

L, suprasternal notch to upper border of pubes.
M, circumference of abdomen at level of umbilicus.
N, circumference of thorax at level of nipples in the male, and just above breasts in the female.
Thighs, $O(P + Q)$, 0.508.
O, superior border of the great trochanter to the lower border of the patella.
P, circumference of thigh just below the level of the perineum.
Q, circumference of hips and buttocks at level of trochanters.
Legs, *RS*, 1.40.
R, from sole of foot to lower border of patella.
S, circumference at level of lower border of patella.
Feet, $T(U + V)$, 1.04.
T, length of foot.
U, circumference of foot at base of little toe.
V, smallest circumference of ankle.

11 (943)

On the law relating milk flow to age in dairy cattle.

By RAYMOND PEARL.

[*From the Biological Laboratory of the Maine Agricultural Experiment Station.*][1]

Before the production records of different cows may be critically compared, as in the study of the inheritance of milk flow, for example, it is necessary to make proper corrections for the differing ages of the individuals compared. It has long been a matter of common knowledge that there is a change in amount of milk produced as a cow grows older. Before any proper corrections for this factor can be applied it is essential to determine with precision, and, so far as may be, generality, the quantitative law connecting these two characters milk flow and age. By the associations and individuals who have in charge the Advanced Registry records in all of the dairy breeds of cattle it is generally, and quite erroneously, assumed that the relation between these two variables is a strictly linear one.

[1] Paper No. 74.

During the past two years I have been engaged (with the assistance of Messrs. John Rice Miner, John W. Gowen, and S. W. Patterson) upon a study of this problem, as a necessary preliminary to a genetic investigation of milk production. The essential result reached may be stated as follows: *The amount of milk produced by a cow in a given unit of time (7 days, 1 year, etc.) is a logarithmic function of the age of the cow.*

The actual curves which were found to graduate successfully the non-linear regression lines in the case of the different breeds were of the general form

$$Y = a + bX + cX^2 + d \log X,$$

where Y denotes the amount of milk produced in a given time, and X denotes the age of the cow. This form of curve is one with which we are already familiar in connection with studies of growth, the change in size of the hen's egg with age, etc.

The law may be stated verbally in the following way: Milk flow increases with increasing age but at a constantly diminishing rate (the increase in any given time being inversely proportional to the total amount of flow already attained) until a maximum flow is reached. After the age of maximum flow is passed the flow diminishes with advancing age and at an increasing rate. The rate of decrease after the maximum is, on the whole, much slower than the rate of increase preceding the maximum.

In general the law above stated applies to the absolute amount of fat produced in a unit time as well as to the milk.

Fitted curves, on which the above statements are based, have been worked out for three of the four important "dairy breeds," and data are in hand indicating that the same general law holds for all breeds of cattle. Detailed reports of these investigations will appear in another place.

12 (944)

A case of diabetes mellitus complicated by alimentary pentosuria and occasional lactosuria.

By JACOB ROSENBLOOM, M.D., PH.D.

[*From the Biochemical Laboratory of the Western Pennsylvania Hospital, Pittsburgh, Pa.*]

The writer has completed a study of certain phases of metabolism in an adult suffering from diabetes mellitus, who also presented a very low tolerance for pentose and for lactose.

13 (945)

Metabolism studies in a case of diabetes insipidus, in a four-year-old boy.

By JACOB ROSENBLOOM, M.D., PH.D., and HARRY T. PRICE, M.D.

[*From the Biochemical Laboratory of the Western Pennsylvania Hospital, Pittsburgh, Pa.*]

For a period of nine days we have studied, in a boy suffering from diabetes insipidus, the nitrogen metabolism and urinary nitrogen partition; the sulphur metabolism and urinary sulphur partition; the calcium, magnesium, and phosphorous metabolism, the chloride metabolism and the fluid intake and output.

The studies were carried out on low and high protein diets and on low and high sodium chloride diets. In some respects the condition seemed to be due to a defect of the kidney to secrete a concentrated urine; in other respects this was not so.

14 (946)

The origin of gastric hydrochloric acid.

By OLAF BERGEIM.

[*From the Laboratory of Physiological Chemistry of Jefferson Medical College.*]

Of the many suggestions brought forward with regard to the chemistry of the process by which the hydrochloric acid of the gastric juice is produced, one by Maley[1] has certain things in its favor which cannot be said of the others. This relates to the interaction of disodium phosphate and calcium chloride with the production of hydrochloric acid and tricalcium phosphate. Probably what really takes place when solutions of these are mixed, is the formation of acid Ca phosphate which hydrolyzes rapidly at room temperature to form a basic calcium phosphate and an acid phosphate containing more phosphoric acid than the monophosphate. The latter may be considered to act upon the calcium chloride with production of free hydrochloric acid. Maley showed that free HCl could be dialyzed from such a mixture, which we have confirmed also by distillation with or without the addition of manganese dioxide. In the former case abundant chlorine is liberated. Fatal objections to the theory in its original form are that there is no adequate supply of calcium chloride in the organism for this purpose and that no provision was made for removal of the insoluble triple phosphate which must be formed. The source of chlorine ions can not be other than the NaCl of the blood. It can be shown that NaCl is decomposed by acid calcium phosphate but not by acid sodium phosphate. That acid calcium phosphate can be produced in the body is indicated by facts given in another place.[2] Nuclei contain much Ca and as this is not present in the inorganic form and as nucleins are with difficulty if at all separated from it, apparently it exists in combination with nucleic acids. This being the case and as phosphonuclease has been shown to be present in nearly all tissues the splitting off of acid Ca phosphate presents no great theoretical

[1] Maley, *Zeit. f. physiol. Chem.*, Vol. 1, p. 174, 1877.

[2] This Journal, 1914, Vol. 12, p. 22.

difficulty. This on hydrolysis in the presence of NaCl would yield HCl. That certain of the leucocytes carry the Ca and P for this process is probable as well as that they serve to carry away the basic phosphate which however would be formed in smaller amounts than corresponds to Maley's conception. Assuming (which is not necessarily the case) that all phosphoric acid were split off as acid Ca phosphate we should expect the gastric juice to contain appreciable amounts of acid Ca phosphate and that this might be roughly proportional to the acidity. The former is apparently correct, while the latter appears from the few cases studied, to be probable.

Confirmatory of this view are the findings of high acidity and efficient digestion associated with hyperfunction of pituitary and thyroid and the opposite with hypofunction. Also the decrease of gastric secretion after parathyroidectomy (Keeton[1]), aided by Ca salt administration; and favorable effect on acid secretion in some achylias of parathyroid treatment (Rehfuss[2]). These presumably act by a stimulation of the nucleolysis necessary for acid production or by mobilizing the acid carrying cells. These relations are still being investigated.

15 (947)

Phospho-nuclease as related to phosphorus and calcium metabolism.

By OLAF BERGEIM.

[*From the Laboratory of Physiological Chemistry of Jefferson Medical College.*]

Studies made in this laboratory of the Ca metabolism in certain ductless gland disturbances have emphasized to us the unsatisfactory nature of the views held with regard to Ca distribution and calcification. In our case of acromegaly[3] with hyperfunction of hypophysis Ca absorption and excretion were marked, the absorption apparently taking place even from the difficultly

[1] Keeton, *Am. J. Physiol.*, 33, 25, 1914.

[2] Rehfuss, unpublished results from this laboratory.

[3] Bergeim, Stewart and Hawk, *J. Exp. Med.*, XX, 218, 1914.

soluble residue in the lower intestine. After parathyroidectomy[1] absorption and excretion were very low. The Ca content of the blood however increased slightly which has been shown for *P* also by Greenwald.[2] There is decreased *P* catabolism but increase in the blood and Ca deprivation of tissues due to impaired excretion. Hyperthyroidism with its nervous symptoms would represent increased catabolism with more normal excretion. The apparent opposition of thyroid and parathyroid is likewise explained by greater catabolism in presence of thyroid than in absence of both.

These facts and a host of others related to endocrinous gland function may be interpreted briefly as follows. The intestinal epithelium and leucocytes invading it (probably the splanchnic basophiles) by virtue of the phosphonuclease they contain liberate from nucleic acid (possibly other phosphoric esters also) phosphoric acid which dissolves Ca phosphate. Ca is carried partly in combination with the leucocytes and is necessary for nucleolytic action. Macallum[3] has shown these cells to absorb and transport iron salts. Westbrook found the cells in extremely large numbers in villi of carnivora, particularly the dog (bone ingestion?).[4] In decalcification of bone the osteoclasts act in a similar manner. In ossification the osteoblasts split off acid Ca phosphate which hydrolyzes to the carbono-phosphate.

The question as to why only certain tissues as cartilage calcify is a distinct problem but may be largely a matter of chemotaxis. As cartilage seems to have a specific adsorption affinity for Ca salts and as Ca salts introduced from without stimulate ossification, Ca salts are probably the agents of the chemotaxis. Likewise in pathological calcification, degeneration with liberation of phosphoric acid in the tissue would lead to primary deposition which would be continued by the leucocytes. Calcification in the embryo chick must be analogous.

The parathyroid must act by stimulating these processes as instanced by parathyroid hyperplasia with osteomalacia and atrophy with rickets, infantilism, osteitis deformans. Interesting

[1] Bergeim, Stewart and Hawk, *J. Exp. Med.*, XX, 225, 1914.

[2] Greenwald, *J. Biol. Chem.*, XIV, 363, 369, 1913.

[3] Macallum, *Jour. Physiol.*, 16, 268, 1894.

[4] Westbrook, *J. Physiol.*, 18, 490, 1895.

is the increased resorption *and* deposition in acromegaly with high P metabolism. Other less essential glands as the thymus apparently act mainly as supplies and stores of nuclein.

The importance of phosphoric acid for oxidation processes as fermentation is readily correlated on this basis with disturbances of carbohydrate oxidation (diabetes, decreased oxidation with hypofunction and increased with hyperfunction of pituitary and thyroid, and other well known examples). As indicated above, as well as by tartrate production of nephritis, excretion by kidneys and intestine as well as maintenance of blood neutrality are much more than simple mass action and filtration processes.

16 (948)

The effect of lead on the germ cells of the male rabbit and fowl as indicated by their progeny.[1]

By **L. J. COLE** and **L. J. BACHHUBER.**

[*From the Department of Experimental Breeding, Wisconsin Agricultural Experiment Station.*]

The experiments of Stockard[2] on guinea pigs and of Cole and Davis[3] on rabbits have shown conclusively that alcohol has a deleterious effect on the germ cells of the male. In the experiments here reported lead, in the form of lead acetate, was substituted for the alcohol, lead being chosen because of its reputed effect upon the offspring of workers, whether male or female, in trades where they are exposed to lead in its various forms. The method of double mating described by Cole and Davis was employed. This consists in breeding a female of a certain type to two males at the same period. The males are of such gametic constitution that the young of each may be identified by color or other characteristics. The experimental animals used were

[1] Papers from the Department of Experimental Breeding of the Wisconsin Agricultural Experiment Station, No. 3.

[2] See especially "The effect on the offspring of intoxicating the male parent and the transmission of the defects to subsequent generations," *Amer. Nat.*, Vol. 47, No. 563, pp. 641–682, 1913.

[3] "The effect of alcohol on the male germ cells, studied by means of double matings," *Science* (N. S.), Vol. 39, No. 1004, pp. 476–477, 1914.

TABLE I.

RESULTS OF BREEDING NORMAL AND POISONED MALES TO NORMAL FEMALES.

(Numbers relating to offspring of poisoned males are in heavy type.)

Series.	Normal Male.	Poisoned Male.	Successful Double Matings.	Unsuccessful Double Matings.	Albino Offspring.			Pigmented Offspring.			Average Wt. at Birth.	
					Total.	No. Dead in 4 Days.	Per Cent. Dead in 4 Days.	Total.	No. Dead in 4 Days.	Per Cent. Dead in 4 Days.	Albino.	Pigmented.
I.....	D.M. 20.2	Alb. 26.8	9	13	**84**	**40**	**47.7**	90	17	18.9	**49.8**	54.7
II.....	Alb. 21.4	D.M. 20.2	5	15	27	8	29.2	**147**	**51**	**34.2**	59.0	**49.1**

rabbits and fowls. The lead acetate was mixed with sugar of milk and fed in gelatin capsules.

A. RABBITS.

Two series of experiments were run. In the first (I) a normal homozygous Dutch-marked male (♂ 20.2) and a poisoned albino male (♂ 26.8) were both bred to a number of albino females. In the other series (II) an albino male (♂ 21.4) was used as the normal or control animal, while the previous control male (Dutch ♂ 20.2) was subjected to the lead treatment. The results from the two series are shown in Table I.

A comparison of the two series shows: (1) The mortality of the albino young within four days after birth dropped from 47.7 per cent. when the albino male (♂ 26.8) was poisoned to 29.2 per cent. in those young which came from the normal albino male (♂ 21.4). (2) The mortality of the pigmented young in the same period rose from 18.9 per cent. in Series I, when the pigmented male (♂ 20.2) was normal, to 34.2 per cent. in Series II, after he had received the lead treatment. (3) Coincident with the lower death-rate in the albinos in Series II over those in Series I, it will be noticed that there is a distinct rise in the average weight of the young at birth—from an average weight of 49.8 grams when the father was poisoned to 59.0 grams when the father was normal. (4) The average weight of the young of the pigmented male before he was given the lead was 54.7 grams; after the treatment the average weight of the young produced dropped to 49.1 grams. In this connection it should be mentioned that both albino males were considerably larger than the Dutch (♂ 20.2), the former varying around about 2,900 grams, while the latter averaged only about 2,100 grams. In spite of this his offspring averaged larger than those of the poisoned albino male.

From the foregoing it seems legitimate to conclude that the offspring produced by male rabbits which have been poisoned by the ingestion of lead acetate into the alimentary tract have a lower vitality and are distinctly smaller in average size than normal offspring of unpoisoned males.

B. FOWLS.

An experiment similar to that with the rabbits has been conducted with fowls. Twelve White Leghorn hens were divided into 3 lots of 4 hens each. Those in the first lot were bred only to a White Leghorn cock which was being fed each day a certain quantity of lead acetate; those in the second lot were bred to a normal Houdan cock alone; while the hens in the third lot were bred on alternate days to the Leghorn and to the Houdan. It will be noted that color, comb and toe characters could all be utilized in distinguishing the chicks of the respective cocks. The results obtained with these three lots are tabulated respectively in Tables II, III, and IV. Hen 122 of the second lot and hen 259 of the third lot are omitted from the tables since the former laid no eggs and the latter laid only 3, all of which were infertile.

Inspection of Table II shows that of the 174 eggs obtained from hens mated to the poisoned Leghorn cock 27 per cent. were infertile, 27.5 per cent. of the embryos in the 127 fertile eggs died before hatching, and of the 92 chicks hatched 13, or 14.1 per cent., died before reaching the age of three weeks. Comparing these results with those from the normal Houdan cock (Table III) we find the percentage of infertile eggs in the latter case is much higher, being 42.3 per cent. as against 27.5. On the other hand the percentage of dead embryos (17.2 per cent.) is not much more than half as great and the percentage of chicks dying within three weeks (3.7 per cent.) is only about one fourth as high as in the case of the poisoned male.

The data from mating both cocks alternately to the hens in the third lot (Table IV) corroborate the results shown in Tables II and III. In all 109 eggs were laid, of which 42.1 per cent. were infertile. In 17 of the fertile eggs the embryos died before hatching. Only 10 of these could be identified, there being 9 Leghorns, from the poisoned cock, and 1 crossbred, of non-poisoned Houdan paternity. Of 46 chicks hatched 31 (67.4 per cent.) were Leghorns, but of these 5 (16.1 per cent.) died within three weeks while all of the crossbreds survived that period. These results are interpreted as indicating that in fowls also poisoning of the male parent with lead results in offspring of a distinctly lower average vitality.

TABLE II.

RESULTS FROM FOUR WHITE LEGHORN HENS BRED TO POISONED LEGHORN COCK.

Hen No.	Total Eggs.	Infertile Eggs.	Per Cent. Eggs Infertile.	Dead Embryos.	Per Cent. Fertile Eggs Dead.	No. Chicks Hatched.	No. Chicks Dead in 3 Wks.	Per Cent. Chicks Dead in 3 Wks.
65	60	8	13.3	16	30.7	36	5	13.9
66	36	18	50.0	8	44.4	10	2	20.0
A23	49	3	6.1	6	13.0	40	5	12.5
162	29	18	62.0	5	45.4	6	1	16.6
Totals.....	174	47	27.0	35	27.5	92	13	14.1

TABLE III.

RESULTS FROM THREE WHITE LEGHORN HENS BRED TO NORMAL HOUDAN COCK.

Hen No.	Total Eggs.	Infertile Eggs.	Per Cent. Eggs Infertile.	Dead Embryos.	Per Cent. Fertile Eggs Dead.	No. Chicks Hatched.	No. Chicks Dead in 3 Wks.	Per Cent. Chicks Dead in 3 Wks.
61	44	14	31.8	6	20.0	24	1	4.1
493	33	13	39.3	3	15.0	17	1	5.8
A272	34	20	58.8	2	14.2	12	0	0.0
Totals.....	111	47	42.3	11	17.2	53	2	3.7

TABLE IV.

RESULTS FROM THREE WHITE LEGHORN HENS BRED ALTERNATELY TO POISONED LEGHORN COCK AND TO NORMAL HOUDAN COCK.

(Numbers relating to offspring from poisoned cock in heavy faced type.)

Hen No.	Total Eggs.	Infertile Eggs.	Per Cent. Eggs Infertile.	Dead Embryos.	Identified.		Chicks Hatched.			Leghorns Dead in 3 Wks.	Per Cent. Leghorns Dead in 3 Wks.	Cross-breds Dead in 3 Wks.	Per Cent. Cross-breds Dead in 3 Wks.
					Leghorn.	Cross-bred.	Leghorn.	Cross-bred.	Per Cent. Leghorns.				
A286	47	18	38.3	6	**3**	0	**17**	6	**73.9**	**2**	**11.7**	0	0.0
483	36	12	33.3	7	**4**	1	**13**	4	**76.4**	**3**	**23.0**	0	0.0
157	26	16	61.5	4	**2**	0	**1**	5	**16.6**	**0**	**0.0**	0	0.0
Totals...	109	46	42.1	17	**9**	1	**31**	15	**67.4**	**5**	**16.1**	0	0.0

17 (949)

The action of pituitrin on the secretion of the mammary gland.

By SUTHERLAND SIMPSON and R. L. HILL.

[*From the Department of Physiology and Biochemistry, Medical College, Cornell University, Ithaca, N. Y.*]

The administration of pituitary (posterior lobe) extract to a lactating animal by subcutaneous, intramuscular or intravenous injection causes an increased flow of milk from the mammary gland. In view of the fact that the response is so rapid (the latent period is usually from 20 to 30 seconds) it would not be unreasonable to suppose that the extract acts on the non-striped muscle of the gland, causing an expulsion of the milk already there, rather than on the secretory mechanism, leading to an increased production of milk.

Pituitary extract is known to contain a substance which excites non-striped muscle generally. The ducts and lactiferous sinuses of the mammary gland contain non-striped muscle and it is claimed by some that this tissue is also represented in the alveoli.

To determine whether the flow of milk which follows the intravenous injection of pituitrin is due to stimulation of plain muscle the following experiment was performed. A lactating female dog was anesthetized, cannulæ were introduced into the carotid artery and femoral vein, and the milk-flow recorded on a revolving drum by the exudation method of Schäfer and Mackenzie,[1] a blood pressure tracing being taken at the same time. One c.c. of a 1 per cent. solution of barium chloride was injected into the femoral vein; this was sufficient to produce a marked rise in blood pressure and a slowing of the heart, but there was no increase in the rate of milk flow. Shortly afterwards 1 c.c. of Parke, Davis & Co.'s pituitrin was injected into the vein; this was followed by a rise in blood pressure and at the same time a copious flow of milk.

This simple experiment would seem to prove that the action of pituitrin on the mammary gland is secretory rather than muscular.

[1] Schäfer and Mackenzie, *Proc. Roy. Soc.*, B, Vol. 84, 1911, p. 16.

18 (950)

The reactions of the melanophores of amblystoma larvæ.

By HENRY LAURENS.

[*From the Osborn Zoölogical Laboratory, Yale University.*]

The reactions of the sub-epidermal melanophores, in intact and in isolated pieces of skin, to various stimuli,—light, temperature, solutions of various salts and drugs and electric currents—were studied.

The melanophores of normal and eyeless larvæ[1] react to light by expanding, and to darkness by contracting. If the normal larvæ are, however, kept in bright diffuse daylight on an indifferent background for more than 3 to 5 days the melanophores secondarily contract. Likewise if they are kept in darkness for more than 5 days the melanophores secondarily expand. These secondary responses are lasting and are not shown by the melanophores of eyeless larvæ.

When larvæ are blindfolded, instead of their eyes being removed, the melanophores react to light like those of blinded individuals, that is, they expand and remain so; but they react to darkness like those of normal seeing larvæ, that is, they at first contract, but after 5 days or more they expand.

The melanophores of isolated pieces of skin do not react to daylight, to the light from a Nernst glower, or to darkness. The light from an arc lamp, however, causes them to contract.

From an additional series of experiments on larvæ in which the central nervous system had been partially or totally destroyed it is apparent that the primary responses of the pigment cells to light and darkness are caused essentially by direct stimulation. The secondary responses of the seeing larvæ are, on the other hand, due to nervous activities set up by the stimulation of the retinæ, the stimulation of sensory nerve endings in the skin playing no part.

A high temperature (above 38°) causes the melanophores to

[1] The optic vesicles were removed from the larvæ at the stage of development when the tail bud is just appearing (see Laurens, *Jour. of Exp. Zool.*, XVI, 2, p. 195, 1914).

contract, a low temperature (below 12°) causes them to expand, both in the intact skin and in isolated pieces. These high and low temperatures inhibit the effects of light and darkness respectively. Intermediate high temperatures (above 32°) hasten the rapidity of the contraction and retard that of the expansion of the melanophores, while intermediate low temperatures (between 12° and 17°) have the opposite effects.

Chloretone (0.02 per cent. and 0.01 per cent.) causes the melanophores in the intact skin and in isolated pieces to expand. Curare (0.2 per cent. and 0.1 per cent.) and atropin sulphate (1 per cent.) have the same effect when larvæ are placed in them, but have no effect on the melanophores of isolated pieces of skin.

The injection of a 1 per cent. solution of curare into the body cavity does not affect the primary responses of the melanophores to light and darkness, although the larvæ are rendered immotile, nor does the injection of a 0.01 per cent. solution of nicotine have any effect. On the other hand the injection of a 1 per cent. solution of strychnine causes the melanophores to contract.

An induced current causes the melanophores of normal larvæ, of larvæ in which the central nervous system has been destroyed, of excised portions of the body and of isolated pieces of skin, to contract. A constant current causes them to expand.

The melanophores of *Amblystoma* larvæ do not change their state after the death of the animal, and there is no center for the contraction and expansion of the pigment cells. Nevertheless, the melanophores are under both spinal and sympathetic nerve control as is shown by experiments on larvæ the nervous systems of which were variously operated upon.

ABSTRACTS OF THE COMMUNICATIONS, PACIFIC COAST BRANCH.

Fifth meeting.

San Francisco, California, October 7, 1914.

19 (951)

Note on the reëstablishment of a tendency to metastasize in a Flexner-Jobling carcinoma.

By THEO. C. BURNETT (by invitation).

[*From the Rudolph Spreckels Physiological Laboratory of the University of California.*]

Owing to a misunderstanding on the part of the attendant, our strain of Flexner-Jobling tumor, which had been carried through nine generations since our experiments with cholesterol,[1] was destroyed during the Christmas holidays (1913). In order to repair this serious loss, we asked Dr. Peyton Rous for a new supply, that we might have tumors for future work. He very cordially responded to our demands, as was to be expected, but informed us that his strain had never metastasized, and expressed doubt as to the value of the tumors on that account.

February 21, 1914, we inoculated forty-seven white rats with the new tumor, which was Rous's twenty-first generation, new series. On March 14, thirty-nine, or eighty-three per cent., had well-marked tumors. Twenty-six of these were kept as "stock" and also served as controls, while thirteen were injected four times, at intervals of two or three days, with one cubic centimeter of a 2 per cent. emulsion of cholesterol. The injection was made on the opposite side to that of the tumor inoculation. By April 11 the tumors began to break down, and we were therefore obliged to kill some of the animals. By May 15 all had been killed. A post mortem was made on each rat, and the results were as follows:

Control rats.....26 killed, 9 metastases; 38.5 per cent.
Treated rats (cholesterol)...12 killed, 9 metastases; 75 per cent.

A portion of one of these metastases was fixed and sectioned in

[1] Robertson and Burnett, *Jour. Exp. Med.*, Vol. 17, No. 3, 1913, p. 344.

the usual way, and the diagnosis confirmed microscopically by Professor G. Y. Rusk, of the department of pathology. In addition, seven rats were inoculated with pieces of a metastatic tumor from the mediastinum, and in fourteen days all had developed well-marked tumors.

Two facts seem evident. The tumor has again become a metastasizing tumor, and treatment with cholesterol has increased that tendency. The results from the treatment with cholesterol were to be expected from our former experiments. Why the tumor should spontaneously become more virulent (if we look upon the formation of metastases as an index of virulence) is not so clear. Haarland[1] has shown that mice transferred from Berlin to Christiania became refractory to Ehrlich's sarcoma, and explains it as due to change of diet from fats and proteins, to carbohydrates. This is in accord with the results of Van Alstyne and Beebe,[2] who find a non-carbohydrate diet of casein and lard reduces both the number of "takes" and the growth of the tumor. On the other hand, Danysz and Skszynski[3] found a greater number of "takes" in animals fed on a vegetable diet, than in those fed on meat. Sweet, Corson-White and Saxon,[4] using the Osborne-Mendel diet, which contains plenty of carbohydrate, found a retarding influence. Our rats have been fed the regular laboratory diet of rolled barley, bread, meat, and occasionally lettuce, of which they seem to be very fond. It would seem, then, rather difficult to explain this change in the tumor on the ground of a change in diet.

As to the strain of rats used, they were obtained from New York, and were all over one year of age. This fact may be significant.

There is another possibility that might be tentatively considered, namely, that in all these results of experimental diets we may be dealing with a common factor. If, as has been suggested, cholesterol is a cleavage product of some of the proteins, it may be we shall find here an explanation of some of the varying results of investigators. The diet used by Sweet, Corson-White

[1] Haarland, *Berl. klin. Woch.*, Vol. 44, 1907, p. 713.

[2] Van Alstyne and Beebe, *Jour. Med. Research*, Vol. 29, No. 2, 1913, p. 217.

[3] Danysz and Skszynski, *Compt. Rend. de Soc. de Biol.*, Vol. 74, 1913, p. 1144.

[4] Sweet, Corson-White and Saxon, *Jour. Biol. Chem.*, Vol. 15, No. 1, 1913, p. 181.

and Saxon is apparently a cholesterol-free diet and perhaps the same can be said for casein and lard, although the writer is by no means certain on this point. This is merely suggestive and further investigation along this line may prove it erroneous.

20 (952)

Immunity tests in coccidioidal granuloma.

By JEAN V. COOKE.

[*From the Pathological Laboratory of the University of California Hospital, San Francisco.*]

In a case of coccidioidal granuloma studied no specific complement-fixing bodies or agglutinins could be found in the blood serum using cultures of *Coccidioides immitis* and emulsions of the same organism from human lesions as antigens. No specific skin reaction could be demonstrated. Precipitins, however, could be demonstrated in the serum even when diluted 1–160, when an extract of dried cultures of the organisms was used as precipitinogen. The precipitins were apparently specific since they could not be demonstrated when normal serum was tested with the same antigen or when the specific immune serum was tested with an antigen similarly prepared from the closely related organism *Blastomyces*.

The presence of specific precipitins in this infection must be verified by the examination of other cases. It is suggested that this reaction might be applied as a means of diagnosis in cases of deep seated infection where there are no discharging lesions from which the spherical doubly-contoured bodies can be demonstrated. It might also serve as a means of differentiating coccidioidal granuloma from blastomycosis in obscure cases.

Experiments are now being carried out to determine whether specific immune substances are formed in infected animals.

SCIENTIFIC PROCEEDINGS.

Abstracts of Communications.

Sixty-second meeting.

New York Post-Graduate Medical School. President Lusk in the chair.

21 (953)

Serological analysis of a case of serum sickness in a human being.

By **Richard Weil.**

[*From the Department of Experimental Therapeutics, Cornell Medical College.*]

A case of meningococcus meningitis received 95 cubic centimeters of therapeutic serum derived from an immunized horse, intraspinally. On the eighth day, the patient developed serum sickness, characterized by fever and a rash. These symptoms lasted one week. On the day following the subsidence of the serum sickness, blood was taken from this patient. This blood was shown to contain both antibody to horse serum, and remnants of horse serum itself, by the following procedures:

(*a*) Antibody to horse serum was demonstrated through the fact that the patient's serum passively sensitized guinea-pigs against horse serum, in amounts of 0.15 c.c.

(*b*) Horse serum was demonstrated through the fact that the patient's serum produced a sharp anaphylactic response in guinea-pigs passively sensitized against horse serum by the previous injection of the serum of a rabbit immunized against horse serum. This result is not produced by control human sera.

A second aspiration of this patient's blood made after the lapse of another week failed to demonstrate the presence of antibody; and of horse serum in very small amounts.

These results show that antigen persists in the human being after the serum sickness has subsided. This fact is in harmony with animal experiments. They show that anaphylactic antibody is formed as a feature of serum sickness.

The coëxistence of these factors in guinea-pigs similarly treated, I have demonstrated in previous experiments. Neither factor had as yet been demonstrated in human serum sickness. The facts indicate that the disease is due to the interaction of these factors, in accordance with an hypothesis suggested by Pirquet.

22 (954)

Cellular processes in the latent period.

By RICHARD WEIL.

[*From the Department of Experimental Therapeutics, Cornell Medical College.*]

Guinea-pigs were passively sensitized by the injection of the serum of a rabbit highly immunized to horse serum. Before the latent period had expired, *i. e.*, during the first 12 hours, the guinea-pig was killed, and the horns of the uteri were suspended for graphic tracing. One horn was immediately tested by means of horse serum. If it gave no response, the preparation was at once thoroughly washed, and the experiment continued. Both horns were kept in Locke's fluid for several hours. At the end of this time, both were again tested against horse serum. Both regularly responded with contractions, but that yielded by the previously tested horn was much less vigorous than by the other. The latter fact shows that the preliminary test by horse serum had partially desensitized the antibodies.

The following conclusions are drawn:

1. The cells absorb antibody from the blood during the first stage of the latent period. These antibodies can unite with the antigen, and the cells can thus be desensitized, but that this reaction produces no cellular contraction in the sensitized muscle cells.

2. The cells "activate" the absorbed antibody during the

second stage of the latent period, in such wise that the reaction with antigen produces a cellular stimulus, with muscular contraction in case of the uterus. It is for this reason, that the combination of antigen and antibody in the blood never produces an anaphylactic response.

The "activation" by the cells also greatly increases the avidity of cellular antibody for antigen, as has been shown in previous papers. Exactly the same features differentiate cellular from circulating antibodies after active sensitization.

23 (955)

A test for antithrombin in the blood.

By **ALFRED F. HESS, M.D.**

[*From the Research Laboratory, Board of Health, New York City.*]

The method of testing for antithrombin in the blood is at present very difficult, as it requires the preparation of a pure fibrinogen containing no prothrombin, that is to say, which does not clot upon the addition of calcium, and also the preparation of a pure thrombin which can be made from fibrin. As a result the method is hardly adaptable to general clinical use.

For some time I have employed a method which seems to meet this difficulty. For this purpose about 9 c.c. of blood are aspirated and put into 1 c.c. of 1 per cent. sodium oxalate. The blood is centrifugalized and the plasma siphoned off in the usual way. The plasma is then recalcified by adding 2, 3, 4 and 5 drops respectively of a ½ per cent. calcium chloride solution. In this way we ascertain the general coagulability of the plasma which is the composite of a number of factors,—prothrombin, fibrinogen and antithrombin, and we determine the optimal amount of calcium for this particular plasma. If we heat some of this plasma to 60° C., the prothrombin, as is well known, is destroyed and the fibrinogen is coagulated. After filtering off this coagulum, we have a plasma which contains antithrombin. The strength of this antithrombin may be ascertained for clinical purposes as follows:

First from a normal case we prepare human plasma just as we prepared the oxalated plasma which is to be tested. Five drops of this plasma are put into five thoroughly cleansed vials. One of these serves as a control, to the second three drops of the normal antithrombin is added, to the third five drops of normal antithrombin; to the fourth three drops of the antithrombin that is to be tested, and to the fifth five drops of this antithrombin. All tubes are equalized in amount by the addition of normal salt solution and the mixtures are allowed to remain in contact for fifteen minutes. The plasma is then recalcified by the addition of ½ per cent. calcium chloride, the number of drops which are to be added being determined by the previous coagulability test which should always precede the antithrombin test. As a rule,

TABLE I.

ANTITHROMBIN TEST.

Normal			Hemophilia		
Control	3 Anti.	5 Anti.	3 Anti.	5 Anti.	
—	—	—	—	—	2 min.
+	+	+	+	+	4 "
+++	+++	++	+++	++	6 "
		+++		+++	8 "

four drops is the optimal amount. However, it may be that we have to add a different amount for the normal plasma than for the plasma that is being tested. The time of coagulation is then noted in the usual way. Table I illustrates a test of this nature. It reproduces a test in a case of hemophilia and shows that there was no increase of antithrombin as compared to the normal. There is considered to be an excess of antithrombin if the tubes to which three and five drops of antithrombin have been added, are greatly delayed in coagulating, as compared to the normal. The validity of this test has been determined by means of preparing a solution of hirudin of a strength of 1–40,000 or 1–50,000, which about equals the strength of the antithrombin in human plasma, and testing this upon the normal plasma in the same way as we determine human antithrombin. It will be noticed that the prothrombin and antithrombin are not delicately balanced in the blood and that even when we double the amount of antithrombin, the coagulation is hardly delayed.

Table II shows what may be called the *Coagulation Equilibrium* test. This is performed by adding the antithrombin of the test case to its own plasma instead of to the plasma of a normal case. This tells us how delicately the coagulation is balanced. For example in Table II, which is the plasma of the same hemophilia case as in Table I, we see that the coagulation time is markedly delayed by the addition of its own antithrombin. This is not due to an excess of antithrombin, as we have seen from Table I, but simply means that the plasma is in a very stable condition and that a slight excess of antithrombin will prevent its coagulation. If this coagulation equilibrium-test turns out negatively and there is little delay, it serves at the same time as a test for antithrombin and we may deduce that this substance is not increased.

TABLE II.

EQUILIBRIUM TEST.

Control	3 Anti.	5 Anti.	
—	—	—	6 min.
+	+	+	10 "
+++	+	+	12 "
	+++	+	15 "
		++	35 "
		+++	43 "

24 (956)

Studies on the relationship between creatine and creatinine.

By **V. C. MYERS** and **M. S. FINE.**

[*From the Laboratory of Pathological Chemistry, New York Post-Graduate Medical School and Hospital.*]

When muscle tissue is allowed to autolyze, creatine is transformed to creatinine at a constant rate. The velocity of this reaction increases with a rise in temperature, although practically negligible at 0° C. The rate of formation at body temperature is nearly sufficient to account for the daily elimination of creatinine. The velocity of the reaction is increased by acids but not reduced by Henderson's neutral phosphate mixture. Added creatine experiences the same fate as the creatine originally present, while

added creatinine inhibits the reaction, or if added in sufficient quantity causes it to proceed in the opposite direction. Pure solutions of creatine and creatinine experience the same transformations, although much more slowly. On the long standing of pure solutions there seems to be a slight loss in total creatinine (from both creatine and creatinine). This appears to be due in part to a transformation to urea. Whether or not these phenomena are vital factors in the formation of creatinine in the body, we are unprepared to say.

To obtain further light on this point, experiments have been conducted on nephrectomized animals. The creatine and creatinine content of the various body tissues have been determined several days after a double nephrectomy. In certain of these experiments creatine and creatinine have been injected. Somewhat similar deductions may be drawn from our experiments *in vivo* to those *in vitro;* although there are certain differences between the two types of experiments, the significances of which are not as yet entirely clear to us.

25 (957)

Statistics of pellagra in Spartanburg County.

By **J. F. SILER, P. E. GARRISON** and **W. J. MACNEAL.**

[*From the Robert M. Thompson Pellagra Commission of the New York Post-Graduate Medical School and Hospital.*]

Up to September 15, 1914, we have recorded about 1,165 cases of pellagra, which have been recognized in Spartanburg County, S. C., the large bulk of them since 1910. The population of this county in 1910 was 84,000. The comparative study of the distribution of that portion of these cases recorded up to the end of 1913, in respect to geographical location, race, age, sex and occupation, has shown the disease to be most prevalent in the larger centers of population and especially in the cotton-mill villages. Pellagra has been about three times as prevalent among the white population as in the negroes. It was very rare in children under the age of two, uncommon in the five years following puberty in both sexes, and only slightly prevalent in adult males under fifty

years of age. On the other hand, it was enormously prevalent and severe in females from twenty to forty, somewhat less prevalent, but nearly always mild, in children of both sexes from two to ten years, and almost equally prevalent in old people of both sexes. The greatest pellagra morbidity was observed among persons engaged in housework or remaining at home without occupation, indicating that the causative agent or agencies are present in or near the home. Nevertheless, the women mill workers suffered as much as, or even more than, the housekeepers of the same age when due regard is given to the total number of persons thus engaged.

26 (958)

The vascular response in poisoning from diphtheria toxin.

By **H. B. MYERS** and **GEORGE B. WALLACE.**

[*From the Laboratory of Pharmacology, University and Bellevue Hospital Medical College.*]

From recent work it would appear that neither the heart nor the vaso-motor center is the chief factor responsible for the circulatory changes in diphtheria toxin poisoning. The work we have to report is the result of an attempt made to determine what this factor is.

We have studied first the reactions of the larger blood vessels in poisoned animals. This was done in the following manner: At the height of the poisoning, at a time when the blood pressure was extremely low, the animal was killed, sections of various arteries removed and placed in cold Ringer-Locke solution, where they were kept until ready for use. For comparison sections of arteries from an unpoisoned animal were removed and preserved. A strip of artery from the poisoned animal and one of similar size from the corresponding artery of the normal animal were then prepared, placed in a vessel containing fresh oxygenated Locke's solution, and attached to an apparatus for recording contraction and relaxation. To the solution was then added either adrenalin 1 : 1,000,000; barium chlorid 1 gm. : 255 c.c., or amyl nitrite (.1 to .3 c.c. in 250 c.c.) and the contraction or relaxation of the

artery strips recorded. Allowing for individual variations, the results we obtained from a considerable number of experiments showed that there was no appreciable difference in the reaction of the arteries of the poisoned and unpoisoned animals. Both series gave the same contraction from adrenalin and barium and corresponding relaxation from the nitrite. We conclude therefore that neither the vaso-motor mechanism nor the muscle tissue in the larger arteries are affected to an appreciable extent by diphtheria toxin.

In poisoned animals gastro-intestinal symptoms are prominent. These consist of vomiting and severe diarrhoea. A post-mortem examination of the intestines and other organs shows that striking changes have occurred. The pathological picture of the small intestine shows marked injection of the small blood vessels, arterioles and venules as well as the capillaries. The epithelium shows early coagulation necrosis. In the liver the capillaries show a widespread destruction. There are seen small islands of liver tissue surrounded by pools of blood. In the spleen and kidney also there is seen marked congestion of the terminal arteries.

These structural changes in the different organs are highly significant, and the engorgement of the mesenteric vessels would offer a sufficient explanation for the low blood pressure. We have, however, further studied the reaction of these vessels. A loop of intestine, with its blood supply intact, was placed in a plethysmograph and connected to a calibrated recording tambour. Adrenalin chlorid 1 : 10,000 in Ringer's solution was then quickly run into the plethysmograph, thus bathing the intestine, connection with the tambour made and the change in the intestinal volume recorded. The difference in the decrease in volume in a normal loop, contrasted to that occurring in the intestine of an animal given toxin is very striking. Calculated as cubic millimeters decrease in volume per centimeter of intestine, the average decrease in normal loops was 10.17 cm., the extremes being 15.04 and 5.91. The average decrease in poisoned loops was 1.81 cm. the extremes being 4.73 and 0.57.

In view of the marked structural changes in the smaller blood vessels, and of the failure of these to respond in the normal way to adrenalin we conclude therefore that the chief factor concerned

in the circulatory collapse in poisoning from diphtheria toxin is the arteriole and capillary dilatation.

27 (959)

The influence of feeding upon acidosis in the phlorhizinized dog.

By STANLEY R. BENEDICT and EMIL OSTERBERG.

[*From the Department of Chemistry, Cornell University Medical College, New York City.*]

Experiments have been reported by Geelmuyden[1] and by Baer[2] in which they fed protein to dogs under the influence of phlorhizin, and noted a marked drop in the quantity of acetone bodies eliminated in the urine. Lusk[3] has called attention to the fact that the animals used by Geelmuyden and by Baer in their experiments were for the most part, only partially phlorhizinized, and that their results might be explained on the assumption that the protein ingested gave rise to dextrose which was burned in the organism.

In five experiments which we have carried out upon dogs phlorhizinized according to the method of Coolen, we have found a drop of from fifty to ninety per cent. in the quantity of acetone and of oxybutyric acid eliminated, following the ingestion of moderate amounts of protein. A determination of the glucose to nitrogen ratio in the urine showed that the fall in acidosis cannot be accounted for by ascribing it to sugar burned in the organism.

Since acidosis in the phlorhizinized dog can be practically abolished by such an apparently unrelated factor as the ingestion of protein it is obvious that caution should be used in interpreting results of acidosis studies upon phlorhizinized animals.

[1] Geelmuyden, *Zeitschr. f. physiol. Chem.*, 26, p. 381, 1898.

[2] Baer, *Arch. f. exp. Pathol. u. Pharm.*, 51, p. 271, 1904.

[3] Lusk, *Ergebnissee der Physiologie*, 1912, XIII, p. 371.

28 (960)

Atrophy does not involve acceleration of tissue enzyme action.

By MAX MORSE.

[*From the Department of Physiology, University of Wisconsin.*]

The thesis that atrophy, such as occurs in normal involutionary tissue absorption, in muscle whose nerve supply has been severed, etc., involves a change either in autolytic enzyme content or in its activation, is not supported by experiments of the writer. It has been shown by him[1] that in the larval frog, where, during metamorphosis extensive atrophy occurs, the histological picture resembles closely those of polymyositis, dermatomyositis, etc., as described by Strümpell, Jacoby, Steiner, et al., and that in the case of this amphibian, there is no acceleration of autolysis *in vivo* nor *in vitro* and where thyroid is used to accelerate metamorphosis, as Gudernatsch first showed, the time of completion of the process is reduced two thirds; even in this case, there is no change in rate of autolysis. In another set of experiments, the left sciatic of a rabbit was cut under asepsis, the wound healing, as far as it was permitted to go, without bacterial interference; after a week, the muscles affected were compared as to power for autolysis *in vitro* after the method of Salkowski and here, again, no acceleration of rate of enzyme action was determined.

I know of but a few citations in biochemical literature to investigations along these lines. All of these[2] seem to bear out the same conclusion. Grund, for instance, in an experiment similar to the one above, found the ratio residual nitrogen to total nitrogen to be less than one, and while residual nitrogen involves more than products of hydrolysis of muscle proteins, yet the point is significant; at least there is no increase in tannic acid non-precipitable nitrogen as one would certainly postulate if autolysis is increased in atrophying muscle.

The hypothesis is advanced that in atrophying tissue some

[1] PROC. this society, 1912 and 1913; *Amer. Journ. Physiol.*, 36, p. 1, 1915; *Journal Biol. Chemistry*, 19, p. 421, 1914.

[2] Rumpf und Schumm, *Deutsch. Zeitschr. für Nervenheilk.*, 20, p. 445; *Deutsch. Arch. für klin. Med.*, 79, p. 158; Grund, *Arch. f. exper. Path. und Pharmak.*, 67, p. 393.

change, perhaps in the permeability of the muscle, or in the blood supply, permits the rapid drainage of products of hydrolysis to take place, thus gradually reducing the tissues in amount. In some cases, phagocytosis, stimulated by a precedent lesion, assists in the process of transfer of materials. In involution of the mammalian uterus, there may be a different factor at work, for it has been shown by Slemons[1] that a rise of total nitrogen in the maternal urine occurs after birth and that this is likewise true if the fetus is removed by Cæsarian section, pointing to a relation to the involution of the uterus and likewise to acceleration of proteoclastic enzymes, for uteri are notoriously slow in autolyzing. Langstem and Neubauer and Ferroni obtained acceleration in uterine involution. The point is at present being studied in this laboratory.

29 (961)

Note on action of corpus luteum upon the mammary glands.

By ISAAC OTT, M.D., and JOHN C. SCOTT, M.D.

[*From the Physiological Department, Medico-Chirurgical College of Philadelphia.*]

Our experiments were made upon virgin rabbits. The corpora lutea of the cow were rubbed up with sterilized water and injected hypodermically every three days for a month. The rabbits were of the same size. Care was taken that no sepsis ensued by the injection. It was found that the mammary glands enlarged to a considerable extent, more than twice the original size. They also contained milk. Upon their removal after death and hardened, sections were made and stained. Under the microscope there was about a ten-fold increase in the number of glands compared with the occasional ones in the virgin rabbit.

[1] *Bull. Johns Hopkins Hosp.*, 25, p. 195, 1914.

30 (962)

On the refractive index of the serum in a guinea-chicken hybrid.

By RAYMOND PEARL and JOHN W. GOWEN.

[*From the Biological Laboratory of the Maine Agricultural Experiment Station.*][1]

In connection with some biochemical studies on heredity now in progress in this laboratory we desire to record certain results regarding the refractive index of the blood serum of a genus-hybrid produced from the mating Cornish Indian Game ♂ × Guinea Fowl ♀. The measurements were made with a Zeiss Eintauch Refraktometer on the unmodified serum of freshly drawn blood, expressed from the clot by centrifugation.

Our results show that (1) there is a definite, characteristic, and permanent difference between the refractive index of the serum of the fowl and that of the guinea; and (2) that in the hybrid the guinea parent is dominant in respect of the physico-chemical constitution of the blood as measured by the refractive index. Some figures on the point follow:

Source of Blood.	$_nD$
Fowl (*Gallus* sp.)	1.34537
(Mean of data from 10 birds of different hereditary constitutions)	
Guinea (*Numida meleagris*)	1.34184
(Mean from 6 birds)	
Hybrid (*Gallus* ♂ × *Numida* ♀)	1.34179

31 (963)

Application of the serum-skin test to the diagnosis of pregnancy and different pathological conditions.

By J. BRONFENBRENNER.

[*From the Pathological and Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pa.*]

As it was shown in previous communications,[2] the dialyzable substances in the Abderhalden test appear as a result of auto-

[1] Paper No. 77.

[2] See last number of PROC. SOC. EXP. BIOL. AND MED.

digestion of the serum. The study of this process revealed the fact that the substances, resulting from autodigestion of the serum are toxic to homologous animals—and possibly identical with so-called anaphylatoxin. Last year[1] I described a method in which making use of anaphylatoxin formation I was able to diagnose tuberculosis. In this communication I wish to describe an improvement of the method which makes it possible to apply this test not only to tuberculosis, but to any condition where Abderhalden test or complement deviation test could be applied.

The technique is as follows. 2 c.c. of the serum of the patient is injected in the guinea pig and the next day the guinea pig's blood is collected. This blood, containing at the same time complement and antibody (passively transmitted) is allowed to form anaphylatoxin in a test tube by combining it with tuberculin, placenta, tumor tissue or any other substratum, after which the serum is collected and injected into a normal guinea pig. The test can be made by intravenous or intracutaneous inoculation. In the first case one obtains an acute anaphylactic shock, in the second a local reaction as described by me as serum-skin test.

32 (964)

On the tonus of the vaso-motor center in shock.

By **M. G. SEELIG** and **DON R. JOSEPH.**

[*From the Department of Physiology of the St. Louis University School of Medicine.*]

The experiments here reported were designed to show if possible whether the vaso-motor center is paralyzed or shows evidence of any considerable degree of tonus during surgical shock.

White rabbits were used. One superior cervical sympathetic ganglion was removed and the auricularis magnus nerve on the same side cut. The connections of the blood vessels of the denervated ear with the vaso-motor center were therefore severed.[2] Twenty-four hours or more later the animal was etherized and shock induced by opening wide the abdomen, manipulating the

[1] PROC. SOC. EXP. BIOL. AND MED., 1914, XI, pp. 90–92.

[2] Meltzer, *Amer. J. Physiol.*, 1903, IX, p. 57.

abdominal viscera, and by applying cold water. When the blood pressure had fallen to a low level, *e. g.*, 19 to 25 or 30 mm. Hg., the normal ear, that is, the ear still connected with the vaso-motor center was practically always blanched and bloodless. Even with this low blood pressure, however, the vessels of the denervated ear, contained in most cases, definitely though, as would be expected with low blood pressure, slightly more blood than the normal ear. If at this stage a clamp was applied to the abdominal aorta just below the diaphragm the blood pressure in the anterior portion of the body usually rose quickly to a relatively high level, for example, from 18 mm. Hg. before clamping to 75 or 85 mm. Hg. afterward. With this rise in blood pressure there developed a striking contrast in the appearance of the two ears. The vessels of the denervated ear become gorged with blood, while the vessels of the normal ear in almost every case remained practically maximally constricted. If the connection of the vessels of the normal ear with the vaso-motor center was severed, either by cutting the nerves, destroying their conductivity by the local application of ether, or by freezing the nerves with ethyl chloride, the vessels of the normal ear also became widely dilated.

These experiments have shown that at the time when the rabbits were apparently deep in shock the vaso-motor center was not only not paralyzed but was maintaining a tonus in the vessels of the normal ear of sufficient strength to prevent dilatation of these vessels if the blood pressure was raised to 75 or 85 mm. Hg. or in some cases even higher.

SCIENTIFIC PROCEEDINGS.

Abstracts of Communications.

Sixty-third meeting.

Rockefeller Institute for Medical Research. President Lusk in the chair.

33 (965)

Observations upon the so-called food intoxication of infants with especial reference to the alveolar air.

By **John Howland** and **W. McK. Marriott.**

[*From the Department of Pediatrics, Johns Hopkins University.*]

There is a condition which has been described under the heading of "Food Intoxication" and "Toxicose" in infants, which is a very fatal one. It is found in the course of severe diarrhoeas and as the terminal stage of various disturbances of nutrition. It is characterized by several striking symptoms, chief among which are dyspnea and excitement, changing into stupor and eventually coma. In its early stages, the condition is difficult to recognize. When it is marked it is unmistakable.

The observations which we have to report were made with the desire of learning more with regard to the essential causes of the condition and of developing some method by which it could be recognized in its incipiency when successful therapy is possible.

It was suggested many years ago by Czerny that acids might have some part to play in it for the reason that the dyspnea resembles that seen in rabbits when given mineral acids and the condition has been often spoken of as acidosis, meaning thereby an increase in the acetone substances. These, however, have not been found to be in excess.

For the last two years we have examined the blood of children

suffering from this condition according to the method described by Sellards which consists in evaporating to dryness, with phenolphthalein, the blood serum from which the proteins have been removed by absolute alcohol. A colorless residue indicates an almost complete absence of carbonates from the blood. Marked cases of intoxication show the carbonates to be very greatly reduced in every single instance. In mild cases this is not found to be the case.

Sellards' other method of determining acidosis,—that is, proving a great tolerance to alkali before the urine becomes alkaline, is also striking with these children.

As a more delicate test we have determined the carbon dioxide in the alveolar air. This has never before been determined in infants or young children. It is obvious that the Plesch method, or the rebreathing of air from a bag, is the only available method with infants. The Haldane or the Krogh-Lindhard methods that require either coöperation on the part of the patient or slow breathing are impossible. It is a matter of indifference whether we obtain the true alveolar air or not, so long as we obtain figures which with the individual patients are constant and so long as they fall within reasonable limits with a group of normal patients.

NORMAL

	CO_2 Mm.		CO_2 Mm.		CO_2 Mm.
I	44.6	VII	44.7	XIV	38.4
II	43.5	VIII	41.0	XIV	40.4
III	44.5	IX	39.0	XIV	38.4
III	44.3	IX	38.0	XV	40.4
III	44.5	IX	38.2	XVI	41.3
IV	39.0	X	38.9	XVI	39.6
IV	38.4	XI	40.3	XVI	40.0
V	40.2	XII	39.6	XVII	39.8
V	43.6	XII	41.7	XVIII	39.6
VI	40.8	XII	42.2	XVIII	38.7
VI	43.5	XIII	43.4	XIX	41.0

We have found that if a known amount of air is rebreathed for between 28 and 32 seconds and if the respirations are deep and the bag has been well ventilated, that we obtain results from day to day which differ very slightly. We have found that with children that are nearly normal the results are very close to those that Peabody found for adults, that is, that the extreme limits for the

carbon dioxide are 38 and 45 mm., and that the great majority fall between 39 and 42 mm. It is possible to obtain with the same child comparable results from day to day. The difference may be 2 mm.—sometimes more, but usually not so much. Occasionally, one determination is very much too low, but after a certain amount of experience, good results are obtained almost every time.

In contra-distinction to the regularity with the normal patients are the results with those suffering with "intoxication." There is no danger of confusion.

INTOXICATION.

No.	Date.	CO_2 Mm.	Dyspnea.	Alkali.
I	Sep. 22	21.2	+++	given
I	" 23	42.0	0	"
I	" 24	54.0	0	stopped
I	" 24	55.0	0	
I	" 25	41.3	0	
II	Sep. 28	18.0	+++	given
II	" 28	17.8	+++	"
II	" 29	21.3	++	"
II	" 30	32.8	+	"
III	Sep. 27	27.0	++	given
III	" 28	34.0	+	"
III	" 29	36.0	0	"
IV	Nov. 16	32.8	+	given
IV	" 17	36.8	+	"
IV	" 20	59.0	0	stopped
IV	" 24	48.2	0	
IV	Dec. 2	44.8	0	
V		27.8	++	
VI		30.4	++	
VII		24.4	+++	
VIII		27.0	++	

The chart shows single observations on four patients and a series of observations on four other patients. It will be noticed that the carbon dioxide is almost always very low. The highest that we have found is 33 mm.; in one it was 18 mm. Associated with the low pressure there is almost always great dyspnea. We have given, therapeutically, alkali in large doses by mouth, by rectum and subcutaneously. If the alkali is absorbed there is a rapid improvement in the dyspnea and coincident with this a marked rise in the carbon dioxide tension,—in several instances to a point much above normal (up to 59 mm. in one case). When

the alkali is stopped, the carbon dioxide sinks again to normal limits. We have found this method of much assistance in diagnosis and consequently of great value in the institution of treatment.

A report upon further phases of intoxication will subsequently be made.

34 (966)

Fibrinogen deficiency in hemophilia.

By ALFRED F. HESS, M.D.

[*From the Research Laboratory, Board of Health, New York City.*]

The amount of fibrinogen of the blood seems to vary within wide variations both in man and in animals. In hemophilia there have been some estimations of the percentage of fibrinogen based upon the amount of fibrin obtained after coagulation. However, these data are so divergent as to allow of no satisfactory deduction, quite apart from the fact that they give no information as to the quality of the fibrinogen.

In the estimations of fibrinogen here reported, a functional method has been made use of. Precipitated fibrinogen, made approximately according to the method of Hammarsten, has been added to the whole blood of cases of hemophilia, of purpura, and of normal adults and children. To ten drops of blood, one, two, and three drops of fibrinogen have been added; a fourth tube serving as a control. In this way we are able to ascertain whether the fibrinogen had a complementary action in hemophilia, as compared to the other cases, and also whether it brought the clotting time of the blood close to the normal. In all cases, the fibrinogen had been previously tested with calcium and found not to clot over night upon the addition of a few drops of a ½ per cent. solution of calcium chloride. In three cases of typical hereditary hemophilia, repeated tests showed that the addition of one drop of the fibrinogen solution to the whole blood markedly hastened the coagulation time. In one of these instances, a case of severe hemophilia, the clotting time was reduced by fibrinogen in four consecutive tests from 90 to 13 minutes, from 55 to 14 minutes,

from 106 to 87 minutes, and from 3 hours to 16 minutes. On the other hand, similar tests of three cases of purpura brought about no such result, the coagulation time remaining either the same or being delayed by the fibrinogen. This was true likewise when the fibrinogen was added to normal blood.

There is a significant difference between the clot formation of hemophiliac and normal blood. This can be clearly seen when we compare the clots of the colorless oxalated plasma. The normal clot shows a web composed of radiating threads of fibrin; the clot of typical hemophilia on the other hand is gelatinous and contains a basic material resembling powder rather than fiber.

In view of these results, it is concluded that there is a functional deficiency, qualitative or quantitative, of fibrinogen in hemophilia. This, however, does not seem to constitute the essential defect in this desease, for the addition of fibrinogen was frequently not able to bring the coagulation time to normal, nor does the local application of fibrinogen to the bleeding point bring about effective clotting. It is probable that a deficiency may be associated with other pathological conditions.

35 (967)

Reflex vasodilation is not the cause of the collapsing pulse of aortic insufficiency.

By CARL J. WIGGERS.

[*From the Physiological Laboratory, Cornell University Medical College, New York City.*]

In 1908 Stewart[1] pointed out that the sudden rise and fall of the pulse and the low position of the dicrotic notch, in short the well-know "collapsing pulse" so frequently found in aortic insufficiency, could not be due to a regurgitation for (1) the rapid fall occurred before the dicrotic notch and hence during systole and (2) volume curves of the heart show that very little regurgitation takes place in experimental lesions. The changes were therefore attributed to a reflex vasodilation for (1) this would

[1] Stewart, *Archives of Internal Medicine*, 1908, I, 102.

adequately account for such a pulse; (2) irritation of the aorta without insufficiency *apparently* caused a fall of diastolic without a corresponding fall in systolic pressure; and (3) when peripheral vessels were constricted by adrenalin during insufficiency the normal contour returned.

By producing *temporary valvular lesions*[2] while the aortic pressure curve was being recorded by an optical manometer, the following facts have been shown:—

1. When a lesion is suddenly produced the change in pulse occurs within the time interval of one heart beat, and when normal valve action is restored the normal type of curve *immediately* returns. The changes are too rapid to be attributed to a reflex vasodilation.

2. Irritation of the aorta never produces such a change. The records submitted by Stewart as evidence are clearly due to changes in heart rate.

3. The arterial pressure curve shows that while the pressure falls a little more rapidly in systole so that the pressure at the beginning of diastole is slightly lower, *the chief drop responsible for the large pulse and low diastolic pressure occurs during diastole.* The fact that the chief drop occurs before the dicrotic notch, when records are taken with the Hürthle manometer from animals or with a sphygmograph from patients, can be attributed to instrumental error.

4. These characteristic effects in the arterial pressure curves persist after a large part of the peripheral circulation is eliminated by clamping the thoracic aorta and, contrary to the observations of Stewart, the effect is intensified after adrenalin.

5. Changes in the arterial pulse similar to those found in animals can be obtained from an artificial circulation machine when the peripheral resistance remains unaltered.

These results indicate that the changes of pressure evidently responsible for the collapsing pulse, cannot be due to a reflex vasodilation but are due to a *regurgitation of pressure* into the ventricle, whether with or without an actual backflow of blood requires further investigation.

[2] Wiggers, Du Bois, PROC. OF SOC. FOR EXP. BIOLOGY AND MEDICINE, 1913, X, 87.

36 (968)

A new culture medium for Protozoa.

By Rh. Erdmann.

[*From the Osborn Zoological Laboratory, Yale University.*]

Although there are many media extant for cultivating trypanosomes in test tubes, a satisfactory medium for culture on a slide under a cover glass has hitherto not been described, in spite of the fact that only by the slide method is it possible to study the sequence of changes with the greatest accuracy. The method here outlined makes possible the continued study of the life history of the organism either in prepared culture medium or in inoculated tissue.

As a culture medium the plasma of the host is employed and this is either inoculated with the trypanosomes themselves or used as a medium for the growth in vitro of various infected tissues of the host. I have used the plasma of the rat in studying the development of *Trypanosoma brucei* and have been able to keep the trypanosomes in a normal condition for an indefinite period whereas by the use of Ringer's fluid or blood bouillon the organisms die after a few days.

The plasma was obtained by the method of Harrison,[1] Burrows,[2] and Walton,[3] the latter making adaptations for mammalian plasma. In brief, the blood from the infected rat was taken and put into a small drop of plasma on a cover glass and then this was further diluted with plasma in order to reduce the number of blood corpuscles in the hanging drop which was taken from this. The cover glass with hanging drop was either placed on a depression slide or

[1] Harrison, R. G. Observation on the living developing nerve fiber. Proc. Soc. Exp. Biol. and Med., 1907, Vol. IV, p. 140–46. The outgrowth of the nerve fiber as a mode of protoplasmic movement. Journ. Exp. Zool., 1910, Vol. IX, p. 787–848.

[2] Burrows, M. T. The cultivation of tissues of the chick embryo outside the body. Journ. of the Amer. Med. Ass., 1910, Vol. LV. The growth of tissues of the chick embryo outside the animal body, with special reference to the nervous system. Journ. Exp. Zool., 1911, Vol. X, p. 63–83.

[3] Walton, A. J. Variation in the growth of adult mammalian tissue in autogenous and homogenous plasma. Proc. R. S. L., Ser. B., Vol. 87, p. 452–61.

on a regular slide for study with dark field illumination. In essentially the same way pieces of tissue were placed in plasma under a cover glass and sealed. Precautions to secure aseptic conditions were taken.

This method keeps trypanosomes living, growing and dividing, and thus many of the stages described by various authors either in the host itself or in the transmitter have been studied in vitro. It is evident that this method may be employed not only for blood parasites but for all protozoan forms which are parasites in cells and thus affords another method of approach for the solution of the complicated life cycles of parasitic Protozoa.

37 (969)

The influence of depancreatization upon the state of glycemia following the intravenous injection of dextrose in dogs.

By I. S. KLEINER and S. J. MELTZER.

[*From the Department of Physiology and Pharmacology of the Rockefeller Institute for Medical Research.*]

In former experiments[1] it was shown that after the intravenous injection of large amounts of dextrose (4 g. per kilo) into dogs the sugar rapidly disappears from the blood stream so that after 1½ hours after the end of the injection the blood-sugar falls nearly to its original figure. In the present experiments the same procedure was carried out on completely depancreatized dogs. In these cases the blood-sugar did not fall to its original value or near it; at the end of 1½ hours it was on the average more than twice as high. The following is a comparison of the average figures:

	Blood-sugar.			Dextrose in Urine, Per Cent. of Amount Injected.
	Before Injection.	End of Injection.	1½ Hours After End of Injection.	
Normal (5).....	0.20	0.79	0.27	>43%
Depancreatized (9).	0.38	1.19	0.86	49% (uncorrected for "diabetic" sugar).

[1] See *Proceedings of the American Physiological Society*, Vol. 33, 1913, p. xxvii.

A similar difference was observed also in nephrectomized dogs.

It is claimed by some investigators that the glycemia following depancreatization is due to an over-production of sugar. It is evident that the hyperglycemia in our cases of depancreatization can not be due to such a factor. We shall not discuss here whether our results can be adequately explained by the assumption that the removal of the pancreas causes a decrease of consumption of dextrose by the body tissues. We wish, however, to indicate that some of our facts hint at the possibility of a change in the permeability of the endothelia of the circulatory apparatus as a factor in the results of depancreatization.

38 (970)

The influence of the intra-intestinal administration of magnesium sulphate on the production of hyaline casts in dogs.

By **F. L. GATES.**

[*From the Department of Physiology and Pharmacology of the Rockefeller Institute for Medical Research.*]

Following our study of hyaline cast production after the intramuscular or intravenous injection of hydrated magnesium sulphate and certain other salts, reported to this society in February and June of this year,[1] Dr. Meltzer suggested that the investigation be carried further by a series of experiments in which the $MgSO_4$ was given directly into the intestines, simulating its use as a purgative.

The typical procedure in the present series was to inject an $m/1$ solution of hydrated $MgSO_4$, in doses of .18 or .2 gm. per kilo. body weight, through a glass cannula into the upper duodenum. The small intestine was isolated by ligatures just below the pylorus and at the ileo-cecal valve. The operation was performed under complete ether anesthesia and the dogs were killed at the end of five or six hours. For two animals the solution was diluted to $m/3$ before injection and in three other cases the ligature was not placed at the ileo-cecal valve. In each case control urines were examined for casts and albumin.

[1] PROC. SOC. EXP. BIOL. AND MED., Vol. XI, No. 3 (879); Vol. XI, No. 6 (919).

Of twelve dogs in this series ten showed hyaline casts after the magnesium injection; in eight the casts were abundant. They were usually accompanied by a trace of albumin. The casts were most numerous in the two to three hour period, but usually persisted in small numbers until the end of the experiment. Gross examination of the kidneys revealed no significant changes.

The general effects of the absorbed magnesium appeared in dullness and relaxation, partial or complete anesthesia and paralysis, and in one case in a typical "magnesium death" from respiratory paralysis.

39 (971)

Distribution of solutions in cardiectomized frogs with destroyed or inactive lymph hearts.

By **T. S. GITHENS** and **S. J. MELTZER.**

[*From the Department of Physiology and Pharmacology of the Rockefeller Institute for Medical Research.*]

It has been assumed, in various communications from this laboratory,[1] that the distribution of solutions in cardiectomized frogs takes place by way of a peripheral mechanism. Abel,[2] stated later emphatically that this distribution occurs by the pumping activities of the anterior lymph hearts, stating himself, at the same time, that it would be impossible for the posterior lymph hearts to accomplish such an effect. In opposition to Abel's statement, we demonstrated a year ago,[3] at a meeting of this society, that strychnin is capable of producing convulsions in cardiectomized frogs from which the anterior lymph hearts were previously removed. In a recent paper by Abel,[4] he admits the correctness of our contention that strychnin, etc., may become effective even in cardiectomized frogs without anterior lymph hearts. But now he assumes that the distribution is carried on by

[1] *Jour. of Exp. Medicine*, Vol. 13, 1911, p. 542; *Proc. of Royal Society*, B. Vol. 84, p. 99; PROC. OF SOC. FOR EXP. BIOL. AND MEDICINE, Vols. 8 and 9.

[2] Abel, *Jour. of Pharmacology and Exp. Therapeutics*, Vol. 3, 1912, p. 581.

[3] Githens and Meltzer, PROC. OF SOC. FOR EXP. BIOL. AND MEDICINE, Vol. 11, p. 96.

[4] Abel and Turner, *Jour. of Pharm.*, Vol. 6, p. 91, 1914.

the posterior lymph hearts through some delicate collateral vessels. He is again emphatic in his denial of the possibility of distribution through a peripheral mechanism.

In the last few months we have made several series of experiments on completely eviscerated frogs from which all the four lymph hearts were positively excluded. Thoroughly eviscerated frogs in which in addition the four lymph hearts are especially destroyed, are exposed to extreme shock, which profoundly affects the nervous system. Nevertheless, we have observed in a goodly number of these animals the definite appearance of characteristic tetanic convulsions or of unmistakable hyperesthesia after injections of strychnin.

In another series of cardiectomized frogs which were left on ice for several days, adrenalin was injected into the thigh in doses from 1 mg. to 0.1 mg. In all of these cases definite dilatation of the pupils was obtained—a well-known characteristic reaction to adrenalin. The time before the first effect was noticed varied from ten to thirty minutes. Since the lymph hearts stop beating in a comparatively brief time after cardiectomy, especially when the animals are kept on ice, the distribution of the adrenalin from the thigh to the orbit several days after cardiectomy could not have taken place by the aid of the lymph hearts.

40 (972)

The effect of pituitary substance upon the pulse form of febrile patients.

By **A. W. HEWLETT.**

[*From the Department of Internal Medicine, University of Michigan.*]

In a recent study of dicrotic and monocrotic pulse forms it was shown that these are always accompanied by a transient backward movement of the blood column in the brachial artery just after the entrance of the primary pulse wave. This backward movement may be due either to local conditions in the arm which permit an unusual reflection of the pulse wave or to conditions elsewhere in the cardiovascular apparatus which permit the reflected wave, itself perhaps normal, to become evident on our

tracings. Further observations indicate that this type of pulse is common in fever patients and that it is rarely marked in normal individuals. It is the type of pulse that has frequently been described as bounding, poorly sustained, pointed, etc.—terms which refer to the sudden fall of pressure immediately after the primary pulse wave.

This type of pulse as it occurs in febrile patients may be converted into a normal form by therapeutic doses of a pituitary preparation.[1] Following such an injection the pulse form usually showed a definite change in from ten to fifteen minutes, the maximum effect was reached in about an hour, and the effect did not pass off for two or three hours. The degree of change varied in different patients. Frequently it was so marked that not a trace of the original backflow remained and the pointed character of the volume pulse from the arm was entirely lost. Thus far we have not been able to determine any fixed relation between the change in pulse form and changes in the systolic blood pressure or changes in the rate of blood flow throughout the arm. The change in form however was regularly accompanied by a diminution in the size of the volume pulse in the arm. These changes may be explained by assuming a constriction of the larger arteries in the arm or a constriction of vascular areas elsewhere in the body, particularly in the head and splanchnic region. The pulse changes produced by therapeutic doses of pituitary substance are precisely opposite to those which usually follow a therapeutic dose of nitroglycerin.

41 (973)

The effect of carbon dioxide on the eggs of Ascaris.

By THEOPHILUS S. PAINTER (by invitation).

[*From the Osborn Zoological Laboratory, Yale University.*]

The undivided eggs of *Ascaris megalocephala* (var. *bivalens*) were kept in an atmosphere of carbon dioxide for three months. On the removal of the eggs from the gas, a few smears were allowed to undergo full development. Only about one third of the embryo,

[1] 1½ c.c. of Parke, Davis, and Co.'s pituitrin were injected intramuscularly.

were normal, the remainder being either masses of disorganized cells, or embryos in which the posterior end was differentiated, together with the primordial germ cells. The problem was to determine the causes of the abnormalities. Eggs were preserved in all stages, stained and mounted *in toto*.

Two distinct and independent causes were found for the abnormal development.

The first of these was the fusion of the chromosomes in the equatorial plate phase of the dividing S_1-blastomere. (This is the "Ur-somatic" cell in which the diminution process takes place.) The fusion resulted in one of two things: (*a*) When the fusion involved the greater part of all the chromosomes, the blastomere did not divide. At the next division cycle, a tetraster appeared with eight chromosomes (or their equivalents in small "diminished" chromosomes) lying in the spindles. The tetraster divided very irregularly and the result was the total disorganization of the cells of the ectoderm. Such eggs gave rise to embryos which failed to invaginate. (*b*) When the fusion involved the ends of the chromosomes only, then division took place, but the chromatin was unequally distributed to the two daughter blastomeres, *A* and *B*. This led to an upsetting of the cleavage rhythm of these two cells, the blastomere with less chromatin dividing more rapidly than its mate. The P_1 blastomere (the cell which gives rise to the cells of the entoderm, mesoderm, the stomadeum cells, and the primordial germ cells) and its derivatives divide normally throughout development. It should be added that the P_1 cell plays a dominant rôle in the formation of the posterior end of the embryo. When the division of the chromatin was very unequal, the ectoderm cells became so scattered that they did not take up their proper places and a mass of disorganized cells resulted. When the division was more nearly equal, it seems probable that partially normal embryos resulted.

The second type of abnormality consisted in a shifting of the positions of the *A* and *B* blastomeres and their derivatives. Due to this, the cells from the P_1 blastomere which come into relation to certain of the ectoderm cells to form the stomadeum do not find their proper places. The posterior end of the embryo, coming, for the most part, from the derivatives of the P_1 cell was normally differentiated.

It is interesting to note that while the chromatin of the somatic cell (the one in which the diminution process occurs) is affected by the treatment with the carbon dioxide, the chromosomes of the "Urgeschlechtszelle" are perfectly normal.

42 (974)

Apnea as an after-effect of pulmonary distension and its dependence upon the vagus nerves. Demonstration.

By **T. S. GITHENS** and **S. J. MELTZER.**

[*From the Department of Physiology and Pharmacology of the Rockefeller Institute for Medical Research.*]

In recent years the conception became dominant, due especially to the investigations and teachings of Haldane and his pupils, that apnea as an after-effect of distension of the lung is essentially of chemical origin, due to a reduction of CO_2 in the blood circulating through the respiratory center; this has been designated as apnea vera. It was recently stated that there is no experimental evidence for a possible claim that "true apnea" could depend exclusively upon the intactness of the vagus nerves. At this meeting G. and M. demonstrated the following three facts. (1) A fairly prolonged and complete apnea followed a short distention of the lungs in dogs without any previous artificial respiration; the duration of the apnea depended upon the degree of pressure used for the distension (Meltzer's pleural canula was used for the graphic presentation of respiration). (2) The same apneic after-effect was obtained when the air used for the distension of the lungs contained 5 per cent. CO_2. (3) No such apneic after-effect could be obtained after both vagus nerves were cut.

These experiments demonstrate that the mere distension of the nerve endings of the pulmonary vagus without the aid of a chemical factor (acapnia) is capable of producing a prolonged apnea as an after-effect of the mechanical stimulus. The restriction of the use of the term "true apnea" for a condition produced exclusively by chemical changes does not seem to be well founded.

ABSTRACTS OF THE COMMUNICATIONS, PACIFIC COAST BRANCH

Sixth meeting.

43 (975)

The intra-uterine growth of infants, estimated by the weights of pre- and post-maturely born infants. (Preliminary Communication.)

By **T. BRAILSFORD ROBERTSON.**

[*From the Rudolph Spreckels Physiological Laboratory of the University of California.*]

It has been shown by Read[1] that the intra-uterine growth of the guinea-pig consists of one whole growth-cycle and a portion of a second, birth occurring during the progress of the second growth-cycle. The point of junction of these cycles is a critical period in the growth of guinea-pigs. The junction of the two cycles, at a period when growth is relatively slow, is not infrequently faulty and premature delivery of dead young occurs at this period much more frequently than at any other.

I have sought to ascertain whether or not a similar critical period occurs in the intra-uterine growth of infants. Through the courtesy of the matron, Miss E. C. Sketheway and of Dr. H. Gilbert, I have had access to the extensive and admirably kept records of "The Queen's Home," a large maternity hospital in Adelaide, South Australia.

Reckoning the period of gestation from the date of onset of the last menstruation I find that there is no tendency whatever for premature deliveries, in pregnancies not accompanied by pathological conditions in the mother, to occur at any given period rather than at any other.

Plotting the frequencies of deliveries as ordinates and the corresponding periods of gestation as abscissae we obtain a normal unimodal frequency-curve, the mean period of gestation being 282.5 ± 0.55 days for 247 male infants and 284.5 ± 0.57 days for 264 females, whence it appears that females are born later than

[1] J. Marion Read, *Arch. f. Entwicklungsmech. der Organismen*, 35 (1912), p. 708.

males, the probability of the truth of this conclusion being 142:1.[1]

The weight of the infants at birth increases regularly with the length of the period of gestation. Plotting these weights as ordinates with the corresponding periods of gestation as abscissae the curve of growth thus obtained passes smoothly into the extra-uterine curve of growth for South Australian infants, without any indication of a slackening of growth such as occurs at or near the junction of two growth-cycles. The intra-uterine growth of infants, subsequent to implantation of the embryo, therefore appears to be part of a single growth-cycle which culminates towards the end of the first year of extra-uterine life. At or near this period a junction of growth-cycles (slackening of growth) occurs, and Macgregor[2] has shown that an unusual proportion of infants are of subnormal weight at this period and that these infants are selectively attacked by certain zymotic diseases. This period therefore corresponds with the critical period detected by Read in the intra-uterine growth of guinea-pigs. That it occurs during intra-uterine growth in guinea-pigs and during extra-uterine growth in human beings corresponds with the fact that guinea-pigs are born in a relatively more adult condition of development than man.

44 (976)

The post-natal loss of weight in infants and the compensatory overgrowth which succeeds it. (Preliminary Communication.)

By T. BRAILSFORD ROBERTSON.

[*From the Rudolph Spreckels Physiological Laboratory of the University of California.*]

As stated in the preceding communication, it is possible, by plotting the weights of infants born somewhat before the expiry of the mean term of gestation against the length of the period of gestation, to obtain a curve of intra-uterine growth which continues without any break or any period of loss of weight into the

[1] For the method of computing this probability cf. C. B. Davenport, "Statistical Methods," 2d ed., New York, 1904, p. 14.

[2] A. S. Macgregor "Physique of Glasgow Children," *Royal Philosophical Society of Glasgow Proceedings*, April 21, 1909.

normal curve of extra-uterine growth. It represents the continuation of this latter curve backwards from the time of birth. In the same way, plotting the weights of children born somewhat later than the average term, we obtain a curve which is identical with and overlies the normal curve of extra-uterine growth for the period which it covers. By combining these various data a continuous curve of intra- and extra-uterine growth is obtained without any interruption due to the post-natal loss of weight which normally occurs during the first week after birth. From this we can readily estimate what would be the average rate of growth in an infant during its first two weeks of extra-uterine life were it not for the shock due to birth. For South Australian male infants I find that the gain during the first week following birth should be six ounces, during the second seven ounces. But the average male infant in South Australia actually weighs 6.2 ounces less at one week than it did at birth. Since it should have weighed 6 ounces *more* than it did at birth the true loss of weight due to birth is 12.2 ounces which is 9 per cent. of its weight at birth. At the end of the second week of extrauterine growth the average South Australian male infant weighs 3.4 oz. more than it did at birth, but since it should have gained 13 oz. since birth the loss of weight due to birth is now 9.6 oz. Part of the effect of the shock of birth is therefore overcome during the second week of post-natal life by compensatory overgrowth, for whereas the deficit in weight due to birth at the end of the first week is 12.2 oz., at the end of the second it is only 9.6 oz., *i. e.*, 2.6 oz. of compensatory overgrowth have occurred. Corresponding figures were obtained for females. Hence it appears probable that the average weight of an infant at any given age represents a true dynamic equilibrium, any disturbance of which tends to be rectified by compensatory gains or losses.

The post-natal loss of weight is greater the greater the weight, and, consequently, the size of the infant at birth. It appears probable therefore that the post-natal loss of weight is primarily due to mechanical shock; although defective nutrition and functional shock doubtless contribute to it.

45 (977)

The influence of the anterior lobe of the pituitary body upon the growth of carcinomata. (Preliminary Communication.)

By T. BRAILSFORD ROBERTSON and THEODORE C. BURNETT.

[*From the Rudolph Spreckels Physiological Laboratory of the University of California.*]

We have found that the administration of aqueous emulsions of the anterior lobe of the ox-pituitary, in doses of 0.5 grammes of fresh glandular tissue at intervals of two or three days, either directly into the tumor or hypodermically elsewhere, leads to a very marked increase in the rate of growth of the primary tumor in rats inoculated with the Flexner-Jobling carcinoma. The growth of small tumors is accelerated relatively more than that of large tumors.

This acceleration is only evidenced, however, at a certain stage in the growth of the tumor, subsequent to the twentieth day succeeding inoculations. The administrations do not enhance the tendency of the tumors to metastasize.

Liver-emulsion, similarly prepared and administered, does not cause any acceleration of the growth of carcinomata in rats.

46 (978)

Cholesterol atheroma in rabbits.

By **C. H. BAILEY, M.D.** (by invitation).

[*From the Pathological Laboratory of Stanford University Medical School.*]

The experiments of Ignatowski and Chalatow in which they produced atheroma of the aorta by feeding rabbits on egg yolk or pure cholesterol have been repeated. Each of a series of rabbits was given the yolk of one egg daily mixed with its ordinary food. Other rabbits received daily from 0.2 to 0.5 gm. of pure cholesterol dissolved in cotton seed oil, mixed with their regular food. Three rabbits have thus far come to autopsy: one which had been on an

egg diet for 30 days, one on an egg diet for 77 days, and one on a cholesterol diet for 37 days. All three rabbits show pronounced lesions, the most notable of which are as follows:

In the gross the aorta shows raised irregular yellowish white placques, varying in size from a fraction of a millimeter to several millimeters in diameter. In several cases these are thickly placed and may be scattered over the entire length of the aorta. The pulmonary artery shows similar lesions which in one case are as pronounced as those in the aorta. The liver is of a deep yellow color; the adrenals of a uniform almost white color. The kidneys on section show a deep yellow medulla rather sharply outlined from the brownish red cortex. Very fine yellow lines can be seen in the cortex radiating outward from the medulla.

Microscopically the aorta shows a nodular thickening of the intima made up of large round cells loaded with fat. The inner portion of the media, underlying the intimal lesions, is also involved. Here the fat present is also, for the greater part, intracellular.

The liver shows a marked deposit of fat contained first in the Kupffer cells, later in the parenchymal cells in the centres of the lobules. There is here a focal degeneration of the liver cells. There is apparently a slight increase of periportal connective tissue and fat is present within endothelial cells and fibroblasts in these areas.

The interlobular vessels of the kidney show fat throughout their walls. In the early cases many of the endothelial cells of the capillary network of the medulla are loaded with fat. Fat is also present in smaller amount in some of the endothelial cells of the glomeruli. In a more pronounced case the tubular epithelium shows a large amount of fat.

In the spleen the fat is present mainly in the endothelial cells lining the venous capillaries and in large cells free in the capillaries. The arteries show changes similar to those in the kidneys.

The larger arteries of the lungs show pronounced nodular intimal thickenings similar to those in the aorta. In one case the lining cells of the alveoli contain fat.

In the heart there is a considerable amount of fat in the muscle cells. The fibroblasts of the subpericardial connective tissue and

of the connective tissue trabeculae contain fat. The walls of the small arteries are infiltrated with fat.

The endothelial cells in the organs described appear to be primarily affected. Later the fat is present in fibroblasts in the interstitial tissue and in the parenchymal cells of various organs, as liver, kidney, heart, and lungs. The process in the vessels is not confined to the aorta but involves the pulmonary artery and its branches and the vessels quite generally throughout the organs described.

A small portion of the fat present in the liver is isotropic. The remainder of the fat here and the fat in other situations is anisotropic.

The process evidently reveals considerable difficulty on the part of the rabbit of utilizing the cholesterin fat and as a result the absorption of this fat by phagocytic endothelial cells in various organs and later storage of the same in connective tissue and parenchymatous cells in the organs concerned.

SCIENTIFIC PROCEEDINGS.

Abstracts of Communications.

Sixty-fourth meeting.

47 (979)

The estimation of "acid-soluble" (inorganic?) and lipoid phosphorus in small quantities of serum.

By Isidor Greenwald.

[*From the Harriman Research Laboratory, Roosevelt Hospital, New York.*]

Phospholipins are quantitatively precipitated with the proteins when blood or serum is added to nine parts of a solution containing one per cent. each of acetic and picric acids. The precipitate does not absorb phosphates. This procedure has been combined with the Neumann method of oxidation and the method of Pouget and Chouchak[1] for the estimation of phosphoric acid for the purpose of estimating the "acid-soluble" and the lipoid phosphorus in small quantities of serum (one cubic centimeter or less). The results agree with those previously obtained by other methods upon large amounts of serum.[2] In nephritis, the "acid-soluble" phosphorus may be increased to as much as five times the normal amount. It may also be slightly increased after the ingestion of meat.

[1] Pouget and Chouchak: *Bulletin societe chimique* (4), 5, 104, 1909; 9, 649, 1911.

[2] Greenwald: *Journal of Biological Chemistry*, 14, 369, 1913; *American Journal of the Medical Sciences*, 147, 225, 1914.

48 (980)

The action of certain atmospheric conditions on body temperature and the vascular system.

By FREDERIC S. LEE, D. J. EDWARDS and others.

[*From the New York State Commission on Ventilation.*]

The present research represents a part of an extended investigation, conducted by the New York State Commission on Ventilation, of the physiological action of various atmospheric conditions, especially temperature, humidity, carbon dioxide, and movement of air. Healthy human beings have been confined for periods ranging from 4 to 7 hours in a temperature the air of which can be readily controlled in respect to the desired conditions. A considerable variety of physiological phenomena have been studied and the results will be reported from time to time.

The body temperature of the subjects before entering the chamber was found to be dependent upon the average temperature of the outside air of the previous night, falling and rising as the temperature of the external air rose and fell. The temperature of the chamber itself also influenced the bodily temperature, the latter falling in an atmosphere of 20° C. and 50 per cent. relative humidity, rising in one of 30° C. and 80 per cent. relative humidity, and remaining nearly stationary in air of 23.9° C. and 50 per cent. relative humidity. This is shown in the following record of the results observed in the third series of experiments, 19 to 25 observations for each set of atmospheric conditions, the subjects being confined in the chamber for 7 hours.

Period of Confinement.	20° C. 50 Per Cent. Humidity.	23.9° C. 50 Per Cent. Humidity.	30° C. 80 Per Cent. Humidity.	30° C. 80 Per Cent. Humidity, with Fan Movement.
8.30 A.M.	37.12° C.	36.83° C.	36.86° C.	36.98° C.
3.30 P.M.	36.52° C.	37.02° C.	37.28° C.	37.37° C.

The final average bodily temperatures of all observations to date are as follows:

20° C. 50 Per Cent. Humidity.	23.9° C. 50 Per Cent. Humidity.	30° C. 80 Per Cent. Humidity.
36.73° C.	36.99° C.	37.41° C.

Effects of atmospheric conditions on the circulatory system are best seen when the observed results are viewed in the light of either the Crampton or the Barach indices. The Crampton index is expressed in terms of percentage, which is determined by the increase in the rate of the heart beat and the rise or fall of the systolic blood pressure when the subject passes from a reclining to an erect posture. A high percentage signifies a slight increase in the heart rate and a considerable increase in blood pressure; a low percentage, a marked increase in the heart rate and a considerable decrease in blood pressure. The Crampton percentage rose in an atmosphere of 20° C., 50 per cent. humidity, and fell at 30° C., 80 per cent. humidity, these results signifying respectively an improvement and a deterioration in the circulatory system or its nervous control.

The Barach index of cardio-vascular energy represents the sum of the systolic and diastolic blood pressures multiplied by the heart rate. This fell in air of 20° C., 50 per cent. humidity, while at 30° C., 80 per cent. humidity, it rose above 20,000, the maximum which Barach has assigned to normal, healthy individuals.

The results indicate that as regards bodily temperature and the cardio-vascular mechanism, such a cool and comfortable atmosphere as 20° C., 50 per cent. relative humidity is beneficial, while the heat and humidity of an atmosphere of 30° C., 80 per cent. relative humidity, are deleterious.

49 (981)

Physical analysis of blood serum in nephropathies and cardiopathies.

By **E. E. BUTTERFIELD** and **W. H. BRADDOCK.**

[*From the Pathological Department of Bellevue and Allied Hospitals.*]

The current methods of recognizing renal insufficiency are based on the detection of a diminished rate of elimination of substances normal or foreign to body metabolism. The most reliable data are based on a study of the nitrogen, chloride and

water balance. There are practical and theoretical objections to such studies. Constant diets are impracticable at Bellevue at present and there are too few workers to carry out such investigations on a large scale. On the theoretical side, we know that a diminished rate of elimination of water and chlorides does not necessarily indicate renal insufficiency but may occur in cardiac decompensation with edema.

A diminished rate of elimination must eventually lead to retention and the most accessible place to look for retention is in the blood serum. A complete chemical examination of the serum should reveal the retention of certain substances but in the case of NaCl we know that retention of NaCl and water occur together so that the concentration of NaCl in the serum remains practically constant.

In an attempt to overcome these theoretical and practical difficulties we have worked out a system of physical analysis of the blood serum which has yielded valuable information as to the relative concentration of chemical substances possessing similar physical properties. The freezing point, the refractive index, and the specific gravity of the blood serum are independent variables

TABLE.

	Total Averages.			Extremes.		
	F. P.	$\Delta N_d \times 10^3$.	Sp. g.	F. P.	$\Delta N_d \times 10^3$.	Sp. g.
Normals (5)	0.57	17.4	1.026	0.55–0.59	16.7–18.0	1.025–1.027
Cardiacs with edema (13)	0.56	17.1	1.025	0.53–0.58	15.3–19.2	1.024–1.030
Nephritics with edema (20)	0.56	13.5	1.020	0.53–0.59	11.1–15.7	1.015–1.023
Nephritics with uremia (6)	0.67	18.1	1.029	0.76–0.61	18.9–16.5	1.030–1.027
Nephritics with uremia and edema (3)	0.62	14.3	1.022	0.63–0.61	13.2–15.4	1.020–1.025
Arterio-sclerotics with hypertension (3)	0.57	20.4	1.031	0.59–0.57	20.8–19.7	1.033–1.030

within certain limits. Systematic use of these methods on 50 cases, chiefly nephritics, cardiacs, and arterio-sclerotics, has shown that definite serum pictures exist which are more or less characteristic of different types of nephritic or cardiac disease. Nephritic edema is associated with hydremia while in cardiac edema the blood serum is normal. Uremia may or may not be

associated with hydremia. When hydremia and uremia coëxist subcutaneous edema is also present. The arterio-sclerotic cases with hypertension and with indefinite renal or cardiac symptoms show an extremely concentrated serum without any elevation of the freezing point. The results are easily summarized by giving the numerical values, low and high, and total average for each group.

F.P. denotes the freezing point and Sp.g. the specific gravity of the serum with the usual corrections. $\Delta N_d \times 10^3$ is the difference between the refractive indices of serum and water measured at the same temperature and multiplied by 1,000. The dry residue and the protein content of the serum were also determined. From these determinations it appears that the refractive index depends chiefly on the serum proteins while the specific gravity follows closely the values for the dry residue.

The clinical diagnoses were made by Dr. Van Horne Norrie and Dr. Frank Erdwurm. It is necessary to have thoroughly reliable diagnoses as far as the best contemporary clinical medicine permits. In one case of each of the important groups the clinical diagnoses have been confirmed at autopsy.

50 (982)

The anaphylactic response of the human fallopian tube.

By RICHARD WEIL.

[*From the Cornell Medical School, N. Y. C.*]

The material for this study was obtained in the routine course of gynecological operations, through the courtesy of the surgeons. In the operations for fibroid tumors of the uterus, it is frequently necessary to remove the Fallopian tubes, which furnish a satisfactory basis for the study of smooth muscle reactions. The tubes were studied by the method described by Dale for the uterine horns of the guinea-pig. Some of the material came from women who had previously received horse serum in some form, while in the remainder, regarded as controls, there was no history of the use of diphtheria antitoxin, or other therapeutic serum derived

from the horse. The tubes which came from the sensitized individuals presented a distinct response upon the addition of minute amounts of horse serum, while the controls failed to respond even on the addition of large amounts of horse serum. The contractile response, although much less pronounced than in the case of the guinea-pig, is still unmistakable. The response to ergamine, adrenalin, and other similar drugs, is also very much less marked, in the case of the human preparation. From an anaphylactic standpoint, the human smooth muscle is, therefore, intermediate between that of the guinea-pig and that of the rabbit. This fact explains the character of the anaphylactic symptoms which have been observed in human beings.

51 (983)

The cerebellum in cases of lowered blood pressure and "shock," an experimental study.

By ALFRED REGINALD ALLEN, M.D. (Philadelphia, Pa.).

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The concept of the histology of the Purkinje cell held today by many neuropathologists is but slightly if at all advanced beyond the classification enunciated by Nissl in 1897.

As an introduction to the following work it was necessary to make an investigation of the Purkinje cell in normal animals employing different methods of fixation and staining. It seems desirable therefore not only to state my own views as to classification but also to briefly outline the technique used.

Although monkeys (*Macacus rhesus*), rabbits, cats and dogs were used in this histological study yet the conclusions in this presentation are drawn altogether from the dog.

The animals were all well fed and young. No animal was used which was not in good health. Care was taken to exclude the factor of physical exhaustion. No animal was brought in a shrinking or terrified condition to the operating room. When

everything was ready the dog was quickly overcome with either chloroform or ether.

As soon as the anesthesia was complete the thorax was opened rapidly and a canula introduced into the descending aorta, pointing upward. The right side of the heart was then opened and two liters of Ringer's solution were allowed to flow through the canula. After the Ringer's solution fixation was secured either by Zenker's fluid or by 10 per cent. formaldehyde solution. Followng this the brain was at once removed and placed in Zenker's fluid or 10 per cent. formaldehyde, corresponding to the fixative used for perfusion.

Tissue was mounted both in celloidin and paraffine and stained by many methods. This report is based on the following methods: Eosin-Unna's alkaline methylene blue, the carbol-thionin, Mallory's aniline blue and the hemalum-acid fuchsin. In most cases blocks of tissue were cut so that the Purkinje cell might be studied in three planes.

In describing the following types of Purkinje cells it were well to call attention to some characteristics common to all and also to accentuate the fact that I do not claim that these types represent essentially different entities. This may be so, or on the other hand the different types may represent different stages in metabolic activity of a single entity.

CHARACTERISTICS COMMON TO ALL TYPES OF PURKINJE CELLS.

1. The nucleus is usually oval and its long axis does not necessarily correspond to the long axis of the perikaryon.

2. Excentric placing of the nucleus is found frequently in cells which we must accept as normal.

3. The nuclear cap is a condensation of tigroid material in the form of a crescent which is applied so closely to the nucleus that at times it is difficult to say whether the substance be intra or extranuclear. The periphery of the cap is smooth in the majority of cases. But occasionally a lumpy or torn appearance is found in which event ragged masses of the cap project into the cytoplasm. The nuclear cap stains intensely with the basic dies.

4. The periphery of the nucleus is not necessarily an unbroken oval or circle. In conditions which we must accept as normal

there are frequently found instances of irregularity in nuclear contour. These may amount at times to angular indentations.

5. The nucleolus stains intensely basically but differs somewhat in tint from the chromatin or tigroid substance in that with thionin it appears distinctly a bluish dark blue while the chromatin and tigroid substance with the same stain are of a purple tint.

6. The staining of the primary dendritic trunk is variable in all the types. At times the trunk may be followed easily to its first or second divisions. But in other cells just as normal there is only a very faint indication of the trunk.

TYPES OF THE PURKINJE CELL IN THE DOG.[1]

Type α.—The perikaryon is 25 μ wide and 34 μ long. The nucleus has a mean diameter of 12 μ. The nucleus shows a small amount of chromatin irregularly distributed. The cytoplasm shows a moderate amount of tigroid substance on a light background. This tigroid substance is not arranged as in the anterior cornual cells. The masses are quite irregular in shape and in distribution. Part of the cytoplasm may show little of this substance while in another locality it may be dense.

Type β.—The perikaryon is 22 μ wide and 32 μ long. The nucleus has a mean diameter of 10 μ. Both nucleus and cytoplasm show a dark background. There is about as much chromatin in the nucleus as there is tigroid substance in a field of equal area in the cytoplasm. The arrangement of the tigroid substance is more uniform than in type α.

Type γ.—The perikaryon is 30 μ wide and 35 μ long. The nucleus has a mean diameter of 12 μ. The nucleus shows a small amount of chromatin, irregularly distributed. The cytoplasm has a light background. The tigroid substance is moderate in amount and distributed in a fairly regular manner through the cytoplasm. On account of the moderate amount of tigroid substance the color tone of the cell is light and the nuclear cap stands out in bold relief.

Type δ.—The perikaryon is 30 μ wide and 35 μ long. The nucleus has a mean diameter of 12 μ. The nucleus shows as

[1] The measurements are in all cases approximate only, and are given simply as a guide to those not already familiar with the histology of the Purkinje cell.

small an amount of chromatin as in type γ. The cytoplasm shows a very scant amount of tigroid substance which is distributed with moderate regularity. The granules of tigroid substance are so fine and so few that the cell appears very pale and with too much lighting from the substage may even be missed in a careless examination. At times there is noted near the periphery a thread-like formation of the tigroid substance. In this case the threads run concentrically with the periphery of the perikaryon.

Type ϵ.—The perikaryon is 28 μ wide and 38 μ long. The nucleus has a mean diameter of 12 μ. The nucleus is as in type γ. The tigroid substance is of about the same density as in type γ but the arrangement is peculiar in that the cell appears as if there were an exoplasm and an endoplasm, both clearly defined, and the tigroid substance limited to the latter.

Type ζ.—The perikaryon is 14 μ wide and 45 μ long. The nucleus has a mean diameter of 7 μ. The nucleus and cytoplasm are similar to type β. The cell is often extremely pyknomorphous, even in thin sections. One often finds this type of cell bent almost at right angles or irregularly twisted.

Type η.—The perikaryon is almost circular with a diameter of 15 μ. The nucleus has a mean diameter of 8 μ. The nucleus and cytoplasm appear as in type ζ.

Type θ.—This type of cell is much broader than it is long. It is a very infrequent finding and so far as its staining characteristics are concerned it usually approaches type β.

If one follow the granulo-molecular junction through many folia it becomes evident that there is no definite choice or arrangement of these several types of cells. A succession of from four to ten or twelve type δ cells is a frequent occurrence. To either side of this collection may be found cells of type β. The absence of Purkinje cells over long extents of granulo-molecular junction is of irregular but normal occurrence and is found as frequently at the apex of a folium as in the deep recess of a sulcus.

CLASSIFICATION OF EXPERIMENTAL WORK.

Our animals were subjected to conditions which reduced the blood-pressure markedly for a period of two hours. Moreover in

order to test the theory of possible transmission of centripetal impulses from the periphery to the central nervous system during full anesthesia certain means as noted below were used over prolonged periods. The details of these experiments I shall leave to Dr. Jackson and Dr. Janeway to describe.

In all twenty-two dogs were used. The experiments may be divided into five series, as follows:

Series 1.—Vena cava occlusion and stimulation of both sciatics.

Series 2.—Hemorrhage.

Series 3.—Handling intestines.

Series 4.—Transection of mid-brain anterior to the corpora quadrigemina and handling of intestines.

Series 5.—Transection of mid-brain and stimulation of sciatics.

In series 1 there were thirteen dogs; in series 2 there were four dogs; in series 3 there were two dogs; in series 4 there were two dogs and in series 5 there was one dog.

In the thirteen dogs of series 1 the blood-pressure averaged during the experiment from 34 to 52 mm. The lowest pressure recorded was 20 mm. which was noted in three cases; the highest pressure recorded during these experiments was 70 mm. which was noted in three cases. Eight of the animals in series 1 were killed immediately at the end of the experiment. Two animals were killed six hours after the experiment. One animal was killed five and one half hours after the experiment and two were killed twenty hours after.

In the four dogs of series 2 the average blood-pressure recorded during the experiment was from 34 mm. to 54 mm. The lowest pressure was 20 mm. and the highest 70 mm. All the animals of this series were killed at the conclusion of the experiment.

In the two dogs of series 3 the blood-pressures were in one 150 mm. at the beginning of the experiment and 60 mm. at the end; in the other animal the pressure was 130 mm. at the beginning and 90 mm. at the end. Both dogs were killed at the end of the experiment.

In the two dogs of series 4 the blood-pressure was 80 mm. at the beginning and 30 mm. at the end in one; and 80 mm. at the beginning and 70 mm. at the end in the other. Both animals were killed at the termination of the experiment.

The one dog of series 5 was killed at the end of the experiment. The blood-pressure was not recorded.

RESULTS OF THE MICROSCOPICAL EXAMINATION OF THE CEREBELLA IN THE FIVE SERIES.

I would say that owing to a mistake on my part three of the brains were perfused by a solution of formaldehyde of only a little over 1 per cent. and afterward placed in this weak fixative, I thinking that 10 per cent. had been ordered. These specimens were two in series 1 (S. 155 & S. 158) and one in series 3 (P. 3). These specimens must be discarded from any consideration as post-mortem change is quite evident. In series 1, one specimen (S. 212) has been over differentiated so that new material will have to be prepared before judgment can be passed as to the condition of the Purkinje cells.

This leaves ten specimens in series 1 (S. 140, S. 145, S. 150, P. 1, S. 171, S. 176, S. 184, S. 187, S. 213, and S. 218) on which I would report as follows:

In specimen S. 218 the Purkinje cells show a much greater percentage of type β cell than is normally found. Moreover the pyknomorphous cell predominates. What is possibly furthest from normal is a pronounced vacuolization which one finds in these sections more than occasionally.

It will be noted that the dog of this experiment was not killed until 20 hours after the completion of the work. This is a factor which can not be set aside.

All of the other specimens of this series can be pronounced normal. I would call attention to the gross appearance of the staining in P. 1, which shows well the deeper staining of the paraflocular granules than elsewhere in the cerebellum. This is a normal finding.

In series 2 the following report can be made:—

P. 9 appears normal. This animal's blood-pressure was from 20 mm. to 40 mm. S. 219 appears normal. The blood-pressure in this case was 50 mm. to 70 mm. P. 5 appears normal. The blood-pressure was 25 mm. to 40 mm. Concerning P. 4, Dr. Jackson records on the chart: "Poor transfusion." But this can

not account for the cell picture seen in this case. There are very few type α cells. The number of pyknomorphous cells is very large, as is also the number of type ϵ cells. Very pronounced vacuolization is frequently found. Comparing the sections of this animal with those of others, normal and abnormal, there are noticeably fewer Purkinje cells in P. 4. Of course this can not be explained on the hypothesis of "shock," lowered blood-pressure, damaging action of centripetal stimulation, etc. I do not think anyone would advance the theory that in two hours a large number of Purkinje cells could be absolutely removed. But the question arises, was the animal normal before the experiment? This can not be answered. The blood-pressure of P. 4 was 40 mm. to 60 mm.

In series 3 the following report can be made:—

P. 2 is the only material which need claim our attention. The Purkinje cells are in perfect condition. At the commencement of the experiment the blood-pressure was 150 mm.; at the end of the work it had fallen to 60 mm.

In series 4 and 5 a factor is introduced which we do not find in the other series. I refer to gross traumatizing of cerebral tissue. In each case there is noted: "Poor transfusion." Had we found extensive changes in the Purkinje cells it would have been hard to draw any conclusion. From the ten cases in series 1 and the one case in series 3 I would argue that any marked change in the Purkinje cells was more likely to be due to trauma practically in the immediate neighborhood. As a matter of fact there is little if any more change than is found in S. 155, S. 158 and P. 3.

CONCLUSIONS.

In drawing conclusions from this work we must bear in mind two points. The first is that the baneful effect of serious hemorrhage on the central nervous system has been well recognized for years. Hoche has shown[1] how rapidly the central nervous system is affected by hemorrhage and in the experimental work incident to a paper on "Hemorrhage into the Ventricles"[2] I found how

[1] *Neurol. Centralbl.*, 1895, No. 14, p. 754, and 1900, p. 994; also *Berliner klin. Wchnschr.*, 1900, No. 22, p. 479.

[2] *Journal of A. M. A.*, July 18, 1908.

quickly the cortex of the brain and the lateral columns of the cord lost their faradic excitability in severe hemorrhage. Let us remember this point in considering P. 4, P. 6, P. 7 and P. 8.

The second point to bear in mind is the severity of the stimuli in P. 2.

My conclusions are therefore as follows:

1. Lowered blood-pressure and peripheral trauma such as caused by surgical operations under anesthesia have no demonstrable effect on the Purkinje cells of the cerebellum.

2. The syndrome known as "shock" is totally unconnected with any demonstrable change in the Purkinje cells of the cerebellum.

52 (984)

The influence of nocuous stimuli in the production of shock, and the failure of this influence to support the anoci theory of shock.

By **H. H. JANEWAY, M.D.**

[*From the Department of Physiology, University and Bellevue Hospital Medical College.*]

The experiments reported in this communication have been performed for the purpose of investigating the influence of nocuous stimuli in the production of shock, by comparing with controls the shock-producing effect of severe and prolonged electrical stimulation to the peripheral sensory nerves in animals rendered susceptible to shock-producing influences by a reduction of their blood pressure.

Although an animal may be in severe shock with a high blood pressure, yet a fall of blood pressure always occurs before death and may be regarded as the most striking characteristic of shock. A diminution of blood pressure may, therefore, be legitimately considered to favor the development of shock, in other words, to render an animal a more sensitive test-subject upon which to investigate shock-producing influences. Such a method of experimentation would avoid the difficulty in estimating different degrees of shock in the experimental animals and would permit

the number of deaths of the animals of one series as compared to the results of the experiments of another series in which the animals were rendered slightly less sensitive to shock though subjected to precisely the same severity of stimulation, to determine the increased shock-producing effect of the electrical stimulation of their sensory nerves.

By passing a loop of thread around the inferior vena cava through a small incision in the chest wall, and sewing up the incision in such a manner that the loop of thread emerged in a straight line through the incision, a means was provided of so limiting the amount of blood returned to the heart that the arterial blood pressure could be reduced to any desired degree and for any length of time. At the conclusion of the experiment, one strand of the loop of thread was divided and the loop removed without additional operative procedure, or the danger of pneumothorax, and without any anatomical abnormality remaining.

Such a method furnished a convenient means of reducing the general blood pressure without,—it was assumed,—producing other deleterious effects on the animal than those resulting from the reduction of blood pressure alone. A number of preliminary experiments were devoted to ascertaining the level below which it was dangerous to reduce the blood pressure for a period of two hours. This level was—roughly—40 to 50 mm. of mercury. Having approximately ascertained this level, twelve experiments were performed in which the blood pressure was reduced for a period of two hours, so that the pulse pressure varied

Between 30 to 40 mm. of mercury in 8 animals,
" 20 to 30 " " " " 3 "
" 40 to 50 " " " " 1 animal.

Of these animals, 9 died and 3 recovered. Of the animals which recovered, the pulse pressure of 2 varied between 20 to 30 mm.; and of one, between 30 to 40 mm., for the two-hour period during which the blood pressure was mechanically reduced.

A very important fact which possesses a significance with the true nature of shock, concerns the character of the blood pressure curve after the removal of the loop around the inferior vena cava. The height to which the blood pressure rises immediately after the

release of the ligature is inversely proportional to the fall produced by the ligature. In some dogs it will return to the normal height soon after the experiment and maintain a good height for three to four hours, and then begin to progressively fall until death.

These twelve experiments, therefore, constituted the controls. With them were compared the additional effect produced by strong electrical stimulation of the peripheral sensory nerves in two other series of animals.

In one of these series, the strong electrical stimulation was applied during a period in which the animals' blood pressure was reduced to the same critical degree as in the control series and for the same length of time, *i. e.*, 2 hours. In the second series, the electrical trauma was applied during a period in which the blood pressure was reduced to a level which was considered just above the danger line, *i. e.*, 40 to 50 mm. of mercury.

The electrical stimulation was applied from an inductorium to the central end of both sciatic nerves. By an automatic arrangement, an attempt was made to eliminate block from fatigue and localization, by alternately switching the current from one nerve to the other. All experiments lasted two hours, and this period was selected because it corresponded to the usual duration of a long operation on the human being.

There were 13 experiments in which the electrical trauma was applied during a two-hour period of a low reduction of blood pressure. Of these animals, one alone recovered. In this recovered animal, the pressure varied between 20 to 30 mm.,—in other words, a very low level. Of those that died, the pulse pressure varied

Between 30 to 40 mm. of mercury in 8 animals,
" 20 to 30 " " " " 1 animal, and
" 40 to 50 " " " " 3 animals.

In interpreting the results of this series, some allowance must be made for the greater difficulties of the experiments in the stimulated series as compared with the controls. In the former, much more ether was necessary. Throughout the experiment, even though the animals were unconscious, it was difficult to control the struggling and there was constant hyperpnea; moreover, it

was much more difficult to confine the blood pressure to the desired level.

Comparing this series with the control series, and bearing in mind the modifying considerations which have just been mentioned, the conclusion is justified that little additional shock-producing effect was produced by the electrical stimulation of the peripheral sensory nerves. This conclusion is further strengthened by the results of the second series of stimulated animals. These animals were subjected to electrical stimulation during a period in which their blood pressure was reduced to a level which was considered safely above the critical level of the controls, namely, 40 to 50 mm. Five of these experiments were performed and all animals recovered.

In two of them the pressure was held between 40 and 50 mm. of mercury;

In one, between 40 and 60 mm. of mercury;

In two, between 50 and 70 mm. of mercury.

The results of this series still further emphasize the conclusion that the reduction of blood pressure is the all-important factor in the death of these animals, and that even in animals made very sensitive to shock-producing influences by a reduction of their blood pressure, the additional influence of trauma to the peripheral sensory nerves, as a factor in the death of the animals, is a small one.

In five other similar experiments, an attempt was made to compare the medullary reflexes at the end of the experiment with those at the beginning. In two instances, no increase of the stimulus required to elicit the cardio-inhibitory reflex from central stimulation of the vagus was necessary at the end of the experiment, as compared to the strength of the stimulus required at the beginning of the experiment. In three experiments, such a slight increase was required that it was considered negligible.

53 (985)

Changes in the peripheral circulation following intestinal trauma.

By WALDEN E. MUNS (*by invitation*).

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This investigation had for its purpose the demonstration of the actual changes in the condition of the peripheral circulation following severe manipulations of and trauma to the intestines.

The term peripheral is employed to include the musculature of the extremities and trunk.

Many statements have been made by various investigators as to the actual condition of the peripheral vessels after shock has been brought about by intestinal trauma, but, with few exceptions, such changes have not been clearly demonstrated. Some have apparently concluded that the vessels in the periphery following long-continued intestinal trauma are dilated,[1] while fully as many[2] maintain that this is not true.

RELATION OF TIME, VOLUME AND BLOOD PRESSURE.

Length of Experiment, Minutes.	Fall in Volume at End of Experiment in c.c.	Blood Pressure.	
		Beginning.	End.
52	3	87	70
45	2	110	115
165	5	133	131
120	10	106	105
50	0	91	65
51	9	115	135
92	5 in 31 min., 10, at death	107	118 in 31 minutes

Dogs were used, the anesthetic in each case being ether administered by intratracheal insufflation preceded by physiological doses of morphine and curare. The blood pressure was taken from the carotid artery. A specially made plethysmograph was placed around the leg to above the knee, and was connected with a water manometer which was calibrated. Readings gave changes in volume of the leg.

[1] Mummery, *The Lancet*, 1905, 696; Meltzer, *Arch. int. Med.*, 1908, I, 571.

[2] Malcolm, *The Lancet*, 1905, 573; Seelig and Lyon, *Jour. A. M. A.*, 1909, 52, 45.

The abdomen was then carefully opened along the linea alba and the intestines pulled out. This organ was then handled until a condition of shock was brought about in the animal.

In every experiment except two the water manometer registered a change in leg volume immediately or within a few minutes after the handling of the intestines had begun. In most instances the manipulations of the gut resulted immediately in a slight fall of volume with a fall in blood pressure which was followed in some cases, in a few minutes, by partial or complete recovery of the leg volume to normal. There seemed to be at the beginning of the experiment a period of unstableness of the vaso-motor mechanism in the leg, the arteries being alternately contracted and dilated, without much disturbance in blood pressure.

These variations in leg volume in most cases passed away in a few minutes and the volume tracing from then on showed a gradual fall to the end of the experiment. In one experiment (January 31), the handling of the intestines immediately brought about a slight fall in the volume of the leg with at first a *fall* then a *rise* in blood pressure.

When the handling ceased for two minutes, the leg volume went up, the blood pressure remaining about normal. When the manipulation was taken up again, there was a fall of volume. These transitory changes in leg volume and blood pressure went on through the whole experiment (52 minutes), the general trend of the volume being downward so that at the end of the experiment there was a permanent fall of 3 c.c.

In all cases but one there was a fall of leg volume of from 2 c.c. to 10 c.c.

In all cases but two the blood pressure was maintained throughout the experiment, or at the end was higher than at the beginning.

In the experiment of January 13 where, up to the end, there had been no change in the vaso-motor condition of the leg arteries, as shown by the leg plethysmograph, the blood pressure was 91 mm. Hg at the beginning and had dropped to 65 mm. Hg at the end.

In the experiment of January 31, when the vaso-constriction

in the leg resulted in a 3 c.c. fall, the blood pressure was 17 mm. Hg lower at the end than at the beginning.

In the experiment of December 4, where a 2 c.c. fall in leg volume was noted, the blood pressure rose from 110 mm. Hg at the beginning to 115 mm. Hg at the end of the experiment.

In the two experiments of November 21 and December 13, the fall of volume was 5 c.c. and 10 c.c., respectively, and the blood pressure was exactly maintained throughout the experiments. The time of intestinal handling in the latter experiment was *two hours*, with forty minutes elapsing before any change in volume was noted.

In the experiment of March 18, there was a fall in leg volume of 9 c.c. and a gain in blood pressure of 20 mm. Hg.

In the experiment of January 9, which lasted one hour and thirty-two minutes, the leg volume at the expiration of thirty-one minutes had decreased 5 c.c. and the blood pressure had risen from 107 mm. to 118 mm. Hg. There was a gradual loss of vaso-motor tone in the leg vessels from then on, the leg increasing in volume, the blood pressure showing a steady fall. Within a few minutes of death there was a rapid fall of leg volume, the decrease at death being 10 c.c.

CONCLUSIONS.

Trauma to the exposed intestines brings about a certain vaso-motor response in the blood vessels of the periphery, and this response is a vaso-constriction. This change begins almost immediately that the intestines are disturbed and continues as long as the stimulation is applied.

This reflex vaso-constriction in the peripheral vessels is an important factor in maintaining the blood pressure in cases of gradually developing shock from intestinal trauma, overcoming the blood pressure lowering effect of the splanchnic dilatation. It is shown that whenever the intestinal irritation is not accompanied by vaso-constriction of the peripheral vessels, the blood pressure tends to fall. Whenever the vaso-constriction is present but slightly, the blood pressure shows itself to be better maintained. When the vaso-motor centers can bring about a marked vaso-constriction, the tendency towards the maintenance of the general blood pres-

sure is greater, and in some cases there is actual raising of blood pressure.

Since there is no reason to suppose that the vaso-constrictor center is the variable factor in the difference of vaso-constrictor effect which was obtained, it is reasonable to assume that the results are to be explained by the variation of the normal degree of vaso-constriction present in the periphery at the inception of the experiment. If the vessels were dilated, then reflex constriction could occur to a great extent and aid in the retention of normal blood pressure. If, on the other hand, the peripheral vessels were well constricted, further constriction from trauma would be impossible and the compensatory effect being absent, the blood pressure would fall.

In other words, the effect of intestinal trauma upon blood pressure is determined by the relative degree of constriction or dilatation which exists in the periphery at the inception of the procedure.

54 (986)

Reflex cardio-inhibition in conditions of lowered blood pressure and "shock."

By HOLMES C. JACKSON.

[*From the Department of Physiology, University and Bellevue Hospital Medical College.*]

The experiments reported here represent a continuation and amplification of those presented previously by Ewing and the present author.[1]

In the first series, the accelerator fibers were cut in the dog in order to remove accelerator effects as possible causes for the rise in threshold value of the cardio-inhibitory reflex, observed in conditions of low pressure (hemorrhage, etc.) where the rate of the heart is increased. This factor can be excluded as the same results were obtained as previously published.[1] The second series consisted in an attempt to alter the blood supply of the medulla

[1] Ewing and Jackson, *Amer. Jour. Physiol.*, 1914.

without lowering the general pressure. This was accomplished by ligation of the two carotid and two vertebrals. It is appreciated that even this procedure is incapable of absolutely prohibiting blood from passing to the medulla in dogs on account of the great collateral supply and anastomosis. However, the decrease in blood supply by this method yielded similar results to those obtained in hemorrhage and a reëstablishment of the circulation resulted in a return of the threshold to the normal if the duration of the anemia was not too prolonged. This was comparable to the effect of transfusion following hemorrhage. The third series represents an amplification of the previous work on the effect of trauma upon the cardio-inhibitory reflex. In the early experiments there appeared to exist a parallelism between the blood pressure following trauma and the threshold value for the reflex in the sense that low pressure brought about a high threshold and high pressure, a low threshold. A further study has brought about the conviction that this relationship may exist but that other factors, at present insufficiently studied, alter the results obtained. Following intestinal trauma blood pressure may be high or low according to the initial degree of vaso-constriction;[1] the threshold may be heightened or lowered when the blood pressure is either high or low. One might explain this apparent discrepancy in the findings by the assumption of a factor of inhibition acting independent of the blood pressure and altering the threshold reflexly It is possible, however, that determinations of carotid pressure may not represent accurately the pressure and volume flow of blood in the medullary capillaries. Thus vaso-constriction of the arterioles in the medulla would result in an anemia of that part although the pressure in the carotid might still be normal. It is our intention to examine more closely this phase of the matter.

[1] Muns, PROCEEDINGS SOC. EXP. BIOL. MED., 1915, XII, 87.

55 (987)

The influence of beef fat on growth.

By THOMAS B. OSBORNE and LAFAYETTE B. MENDEL.

[*From The Laboratory of the Connecticut Agricultural Experiment Station and the Sheffield Laboratory of Physiological Chemistry in Yale University, New Haven, Connecticut.*]

The inability of young albino rats to complete their growth on a diet consisting of isolated proteins, starch, "protein-free milk" and lard has directed attention to the need of some substance to supplement the ordinary nutrients so that the characteristic increment in body weight may proceed to its normal limits.[1] Among naturally occurring fats, butter fat, egg yolk fat, and cod liver oil have been shown to be effective as adjuvants to the above artificial dietary in order to promote growth; whereas lard, almond oil, and olive oil behave otherwise. We have now found that *beef fat* is likewise capable of promoting renewal of growth when it has been checked on the lard diets; or if beef fat is incorporated with the food at an early period there is no cessation of growth until long after the time at which nutritive failures on the inadequate diets usually occur.

The content of the growth-promoting substance appears to be smaller in beef fat than in butter fat. By fractional separations it can be obtained in the more liquid portions of the fat—the "beef oil." Beef oil and beef fat, like butter fat and cod liver oil, seem to exert a curative effect in certain affections of the eyes which the rats experience as the result of malnutrition.

A more detailed account of the work will appear in the *Journal of Biological Chemistry*.

[1] Cf. Osborne and Mendel, *Journal of Biological Chemistry*, XV, p. 311, 1913; XVI, p. 423, 1913; XVII, p. 401, 1914; McCollum and Davis, XV, p. 167, 1913; XIX, p. 245, 1914.

56 (988)

The formation of urea in the liver.

By DONALD D. VAN SLYKE, GLENN E. CULLEN, and FRANKLIN C. MCLEAN.

[*From the Hospital of the Rockefeller Institute for Medical Research, New York City.*]

In dogs etherized and operated at various intervals after feeding, we have found the urea content of blood from the hepatic vein to be from 3 to 20 per cent. higher than the portal blood. A similar increase in the urea content during passage of the blood through the muscle tissue of etherized dogs did not occur.

57 (989)

Accurate determination of chlorides in small amounts of blood serum.

By FRANKLIN C. MCLEAN and DONALD D. VAN SLYKE.

[*From the Hospital of the Rockefeller Institute for Medical Research New York City.*]

By the use of an iodometric method under definite conditions one can determine the chlorides in 1 or 2 c.c. of serum with an accuracy of 1 per cent. The proteins are coagulated, and an aliquot part of the filtrate treated with an excess of standard silver nitrate, nitric acid in 5 per cent. concentration being present to prevent precipitation of the purines. A drop of octyl alcohol, which has a faculty of causing colloidal silver chloride to coagulate, is added, and the solution is shaken and filtered. The excess silver in the filtrate is then titrated back with N/50 or N/100 KI, sodium nitrite and starch being present as indicators. The nitrous acid frees iodine as soon as a drop of excess iodide is added, and the blue starch iodate color forms. In order that this end point may be sharp, the solution must have a definite, slight acidity. This is obtained by adding, before the final titration, for each gram of nitric acid present 4 c.c. of a solution containing 446 grams (5/4 gram molecules, 15/4 equivalents) of crystalline trisodium citrate and 19 grams (1/4 gram molecule) of sodium nitrite per liter.

SCIENTIFIC PROCEEDINGS.

ABSTRACTS OF COMMUNICATIONS.

Sixty-fifth meeting.

College of the City of New York, February 17, 1915. President Lusk in the chair.

58 (990)

The influence of sodium salicylate upon the uric acid concentration of the blood.

By **M. S. FINE** and **A. F. CHACE.**

[*From the Laboratory of Pathological Chemistry and the Department of Medicine of the New York Post-Graduate Medical School and Hospital.*]

That the increased output of uric acid following the use of atophan is accompanied by a diminution in the concentration of uric acid in the blood appears to be well established. As has been long known, salicylates induce an increased elimination of uric acid quite comparable to that produced by atophan; and it is of interest to learn whether this urinary increase is accompanied by a commensurate decrease in the blood.

We have found in seven cases that sodium salicylate in daily doses of 6 grams reduced the uric acid concentration of the blood to one half to one third of the initial concentrations.

59 (991)

The effect of thyro-parathyroidectomy on the blood coagulation time in the dog.

By SUTHERLAND SIMPSON and A. T. RASMUSSEN.

[*From the Department of Physiology and Biochemistry, Medical College, Cornell University, Ithaca, N. Y.*]

It has long been held that the parathyroid glands are in some way concerned with the metabolism of calcium in the body. In dogs killed during parathyroid tetany MacCallum and Voegtlin[1] found a decrease in the amount of calcium contained in the blood and brain tissue, and recently MacCallum, Lambert and Vogel[2] have shown that when blood, from which the calcium has, in large part been removed by dialysis, is perfused through an isolated limb, the nerves of this limb show extreme hyperexcitability similar to that observed in tetany.

It is also believed by Wright and others that a diminution of ionic calcium in the blood leads to a prolongation of the coagulation time, and an increase to a shortening of the time.

Our experiments were undertaken with the object of determining whether removal of the parathyroids (and thyroids) in the dog will produce any effect on the speed with which the blood coagulates, and so presumably, point to a change in its calcium content.

We adopted the graphic method of Cannon and Mendenhall[3] of estimating the coagulation time, with one or two slight modifications, and found it to work satisfactorily.

The dog was anesthetized with ether, the left saphenous artery clamped close to the femoral from which it arises, ligatured on the distal side and then opened between the clamp and the ligature. The coagulation tube or canula was made so that it fitted tightly into the central end of the incision, and on relaxing the clamp a sample of circulating blood was obtained. The canula was then plugged with plasticine, quickly removed to a waterbath kept at

[1] MacCallum and Voegtlin, *Jour. Exper. Med.*, 1909, XI, p. 118.

[2] MacCallum, Lambert and Vogel, *Jour. Exper. Med.*, 1914, XX, p. 168.

[3] Cannon and Mendenhall, *Amer. Jour. Physiol.*, 1914, XXXIII, p. 225.

a constant temperature of 25° C. and the time recorded. After each sample of blood had been secured the artery was thoroughly washed out with Ringer's solution.

When ten or more observations had been made, the wound, after being cleansed with corrosive, was closed, and then both lobes of the thyroid (including the parathyroids) were removed. When the symptoms of tetany developed the animal was again anaesthetized and the same procedure adopted on the right limb. At the end of this last experiment it was killed by an overdose of chloroform.

In our later experiments we made three sets of observations on each animal; in the first set the blood was taken from the left saphenous artery, and a few days later, when this wound had healed, the corresponding vessel on the right side was used. At the end of this second experiment the thyroid (including the parathyroids), was removed, and when symptoms developed a third set of observations was made on blood withdrawn from the right lateral circumflex artery, a branch of the femoral arising at a higher level than the saphenous. The object of this procedure was to find out whether, under normal conditions, the coagulation time showed any variation from day to day in the same individual.

Without going into detail, the results of our experiments, so far as they have gone, seem to point to the conclusion that when the symptoms of parathyroid tetany are pronounced (rapid breathing, excessive tonic and clonic muscular contractions, etc.) the coagulation time is prolonged, which may possibly indicate a low calcium content for the blood. On the other hand, where the symptoms are only slight (fine muscular tremors and no rise in body temperature) or just beginning, the coagulation time either remains unchanged or is somewhat shortened.

The following are three examples taken from the thirteen experiments which we have performed:

EXPERIMENT I. DOG ♂, WEIGHT 16.9 KILOS, AGE 13 MONTHS.

1st set of observations (average of 10 readings)—Coag. time 3½ min., normal.
2d " " " " " " " — " " 4½ " "
3d " " " " " " " — " " 6 " during tetany.

In this case the symptoms, which appeared four days after removal of the glands, were very severe: respiration 120, rectal

temp. 104.2° F., marked tonic and clonic muscular contractions.

EXPERIMENT II. DOG ♀. WEIGHT 15.9 KILOS. AGE 12 MONTHS.

1st set of obs. (average of 10 readings)—Coag. time 3½ min., normal.
2d " " " " " " " — " " 4 " "
3d " " " " " 8 " — " " 3 " during slight tetany.

No symptoms appeared until nine days after operation and then only slight muscular tremors were observed with no rise of temperature (100.6° F.).

EXPERIMENT III. DOG ♀. WEIGHT 14.0 KILOS. AGE 12 MONTHS.

1st set of obs. (average of 10 readings)—Coag. time 5 min., normal.
2d " " " " " " " — " " 5 " "
3d " " " " " " " — " " 4½ " after operation.

This dog showed slight symptoms three days after operation. These passed off and did not return and fifteen days later the third set of observations was made after which the animal was killed.

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The relative efficiency of the biological action of the Roentgen rays emitted by the Coolidge and the old type tubes.

By ISAAC LEVIN.

[*From the Department of Cancer Research of the Montefiore Home.*]

In accordance with the modern conception in physics the Roentgen rays present pulsations in the ether analogous to the rays of light. The waves of ether forming the Roentgen rays are considerably shorter than the shortest ultra-violet waves of light. The waves of the so-called soft Roentgen rays are about 1,000 times shorter than those of ultra-violet light, and the waves of the hard Roentgen rays are still shorter.

Any substance, solid, liquid, or gaseous, absorbs a part of the Roentgen rays which pass through it. The fraction of the rays thus absorbed depends upon the density and thickness of the substance. The remaining rays penetrate beyond the interposed substance. The relation between the quantity absorbed by the substance and that penetrating beyond it is of fundamental im-

portance for the proper understanding of the biological action of the Roentgen rays.

When the rays enter a plant or an animal body they injure the cells of the organism through the biochemical action of the rays on the protoplasm and mainly on the nuclei. This biological action differs quantitatively in accordance with the amount of rays absorbed by the cells and the susceptibility of the latter to the action of the rays. When slightly injured a cell may completely recover, while if the injury is severe the cell dies. Every cell of the organism may be killed by a sufficiently large quantity of rays. Nevertheless the biological action of the Roentgen rays must be considered selective in as much as quantities of the rays sufficient to kill a certain kind of tissue may leave adjacent tissues intact or only slightly injured. In order to obtain this selective action the rays must be distributed as evenly as possible through the organism. Such a distribution is possible only with the so-called hard rays, whose penetration is much greater than absorption.

At present there does not exist a direct method for measuring the quantity and the penetration of the rays necessary to kill or injure a given cell. All the measurements are indirect and are based on the fact that the various chemical actions of the rays are also in direct ratio to their quantity. A solution of barium-platin-cyanide which has normally a green color becomes brown under the influence of the rays, and the shade depends upon the quantity used. A photographic paper in black covering will not be influenced by rays of light, but will become blackened under the influence of the Roentgen rays. The shade of black deepens in proportion to the quantity of rays used. On the basis of these color reactions various apparatus are devised for measuring the quantities of the Roentgen rays emitted by a tube in a unit of time.

Before reporting the results of the present investigation a brief outline should be made of the differences in the physical characteristics of the two types of tubes used in the experiments.

Roentgen rays originate on the surface of a metal which is bombarded by the negative electrons of the kathode rays. The greater the velocity of the kathode rays the harder, the more penetrating are the Roentgen rays. The tubes of the old type have an

incomplete vacuum. A high potential current passes in the tube from the anode to the kathode, frees the electrons of the latter and propels them towards the antikathode or target. The bombarding of the electrons induces the formation of the Roentgen rays on the surface of the target. The target is built of platinum and becomes overheated under the action of the kathode rays. The heat frees the gases in the platinum, and these in turn diminish the vacuum of the tube. As a consequence the velocity of the kathode rays also diminishes and the Roentgen rays become softer. Various regulating devices are added to the tube in order to keep the character of the Roentgen rays uniformly hard for a sufficiently long time to produce a biological action. Still the penetration of the rays emitted by the tube constantly changes. The fundamental advantage of the Coolidge tube consists in the fact that it has a nearly complete vacuum so that the small amount of gas escaping from a heated target can not influence it. Moreover the target is built of tungsten which is freed of gas with greater ease before the tube is built. In such a tube with a very complete vacuum high potential current can not pass from the anode to the kathode and free the negative electrons of the latter. The freeing of the kathode rays is accomplished in the Coolidge tube through the heating of the kathode to a very high temperature by the aid of a special storage battery. The kathode consists of a spiral tungsten filament supported by a molybdenum sleeve. The high potential current propels the electrons to the anode, which acts at the same time as a target. The number of the electrons depends upon the temperature of the filament of the kathode and the velocity on the voltage of the primary current.

A priori it could be expected that the Coolidge tube would not only produce a greater output of Roentgen rays, but also generate rays of greater penetrating power. Comparative experiments were done with the best model of tubes of the old type and with the Coolidge tube. Both tubes were placed approximately under similar conditions *i. e.*, the same voltage of primary electric current was sent through the coil, the same number of milliampers of high potential current were sent through the tube, and the resulting Roentgen rays showed the same penetrating power.

To study the distribution of the rays pieces of beef were

radiated and also living animals (pigeons). Test strips of photographic paper (Kienboeck strips) were placed on the surface of the radiated piece and at various depth of tissue. Pieces of meat were used 1, 1½, 2, 3 and 4 inches in thickness. The very soft rays, which usually act only on the surface of the skin of the animal and are not selective but caustic in their action were absorbed by a plate of aluminum 3 mm. thick placed between the tube and the tissue. The pigeons were placed in a box 4 inches deep. One Kienboeck strip was placed over the box and the other under the box. The results of numerous experiments may be summarized as follows:

It takes about ⅓ of the time to obtain the same quantity of rays on the surface with a Coolidge tube as compared with the old type tubes. At the depth of 2 inches of meat the strip shows about ⅓ of the quantity of the rays shown by the surface strip during the same experiment with an old type tube and about ½ by the Coolidge tube. At a depth of 4 inches there is usually about ⅐ of the quantity shown on the surface obtained from a tube of the old type, while from a Coolidge tube one obtains at the same depth usually about ⅕ of the quantity shown on the surface. There is no complete regularity in the results of the experiments with either tube, but the Coolidge tube shows a far greater uniformity. The reason for this difference in the results is probably due to the following: the Roentgen rays emitted by a tube are never uniform in their character and represent all grades of hardness. The methods of measuring the penetration of the tube reveal only the hardest rays. Apparently the rays are more uniform in the Coolidge tube and therefore a greater fraction of those entering the surface reach a certain depth. This feature makes the tube more advantageous than those of the old types. On the other hand it must not be presumed that the rays of the Coolidge tube are greatly superior in their absolute capacity of penetration. As stated above the velocity of the kathode rays and the consequent penetration of the Roentgen rays is in direct proportion to the intensity of the high potential current. The latter can not be increased beyond a certain limit in the Coolidge tube as it is constructed today.

61 (993)

The innervation of the gall-bladder.

By CHARLES C. LIEB and JOHN E. MCWHORTER.

[*From the Department of Pharmacology, College of Physicians and Surgeons, N. Y. City.*]

There are at present two theories as to the innervation of the gall-bladder. One is that supported by Doyon, who claims that the motor fibers pass through the splanchnics; the other theory, which is defended by Dale and Bainbridge, assumes that the motor fibers are derived from the vagi and that the splanchnics carry inhibitory impulses to the gall-bladder.

It seemed that this problem could be definitely solved by a study of the isolated gall-bladder. Although it is impossible in such an experiment to excite the nerves directly by the electric current, the same end result may be brought about by the employment of drugs.

The effects of those drugs which stimulate the para-sympathetic system may be regarded as analogous to the effects following electrical excitation of the vagus. Epinephrine produces the same effect as electrical stimulation of the splanchnic nerves.

The experiments have demonstrated without question that both physostigmine and pilocarpine stimulate the gall-bladder to contract; that atropine promptly removes the action of pilocarpine or physostigmine; that epinephrine, which has a specific action upon the myoneural junctions of the true sympathetic system, produces relaxation of the gall-bladder.

The conclusions that have been arrived at are, therefore, that the gall-bladder receives its motor impulses by way of the vagi and its inhibitory impulses through the splanchnics.

The effects of some other drugs have been incidentally examined. The nitrites and bile salts depress the smooth muscle of the gall-bladder. The excitants of smooth muscle, as represented by strophanthin and barium chloride, produce stimulation of the gall-bladder.

62 (994)

Notes on surgical pathology in the dog.

By **W. HOWARD BARBER** and **JOHN W. DRAPER.**

[*From the Laboratory of Surgical Research and from the Department of Pathology, University and Bellevue Hospital Medical College.*]

1. DIAPHRAGMATIC HERNIA INTO THE PERICARDIAL CAVITY AS CAUSE OF SUDDEN DEATH.

A French poodle, fully grown and bred to extreme fineness, was noticed by his owner, a highly trained observer, to "save himself" in play and for this reason was suspected of having heart-disease. Except for these periods of rest, taken at unexpected and unusual times, the animal appeared physically perfect.

On January 12, 1915, the dog developed general convulsions which lasted one half hour, at the end of which he died. The autopsy, performed the following morning, revealed the following:

1. "*Thorax-Lungs.*—Right slightly congested posterially. Left deeply congested throughout.

"*Heart.*—Pericardial sac large. Right heart compressed by three lobes of liver, gall bladder, and great omentum, 7 by 15 cm. Liver and omentum congested. Gall bladder empty and connected with liver remaining within the abdomen by elongated adhesive band. Deficiency in pericardium measured 3 cm. in diameter and reinforced by fibrous tissue. Deficiency of equal size in central tendon of diaphragm. No hernial sac found.

2. "*Liver.*—Portion within pericardial sac shows extreme passive congestion and fibrosis, indicating that the circulatory obstruction caused by its position has been of long duration. Free portion shows moderate fat infiltration.

"*Edge of Diaphragmatic Opening.*—Appears well rounded and is covered by endothelium,—evidently a congenital defect."

Many phrenic hernias in man have been reported to date.[1] Grosser and Thoma, alone, have collected 433 cases. Leaming's radiograms of Freeman's case[2] showed ante-mortem practically

[1] Keen's "Surg.," Vol. 4, p. 93.

[2] Lockwood, Diseases of Stomach, plate XI, p. 406.

the entire colon in the chest. It entered the mediastinum in front of the heart curving backward over that organ. The liver was transposed. The hernia was through the right side. Besides the true and the false varieties, there is the analogous condition of eventration of the diaphragm. This is defined,[1] as a dislocation cephalad of the abdominal viscera, particularly of the stomach, on the left side under an abdominally high position of the left vault of the diaphragm. The hernia herewith reported is believed to be a congenital true diaphragmatic one, unique, in that part of the liver as well as the gall bladder and the omentum were found within the pericardial cavity.

Respecting the mechanism of such a hernia,[2] Cunningham says: "The diaphragm is occasionally deficient in the human subject producing hernia either through the central tendon into the pericardial cavity or through the lateral portions of the muscle into the thoracic cavity."[3] Keibel and Mall, describing the developments of the body cavities holds, "In the rabbit the pericardial coelom ends in two dorsal and two ventral recesses, all four of which connect subsequently with the peritoneal coelom. However, only the dorsal recesses break into the peritoneal coelom in the human embryo, and it is this recess or canal which later on encircles the lung and probably forms the main anlage of the pleural coelom."

2. BILATERAL NEPHROLITHIASIS AND RIGHT URETERAL CALCULUS.

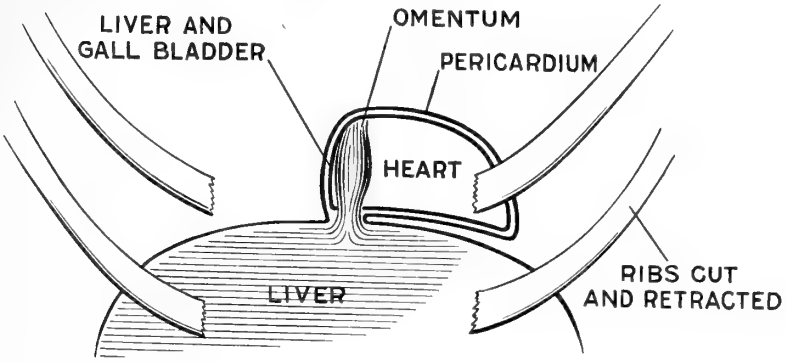
A Dalmatian hound (187 B 2), female, and medium sized had had both ureters transplanted into the sigmoid. The animal lived nine days. At autopsy on the right side a dilated kidney pelvis and a dilated ureter were found. The pelvis contained many small rounded calculi and the ureter a larger elongated stone cephalad to the uretero-colonic anastomosis. On the left side, also, was found a hydronephrosis with a pelvic cast. The ureter on the left side was dilated cephalad only.

This selective ureteral dilatation has been noted several times in a series of uretero-sigmoidal transplantations. An attempt

[1] Sailer and Rhein, *Am. Jr. Med. Sci.*, Vol. CXXIX, p. 688.

[2] D. J. Cunningham, "Text-Book Anat.," Ed. 2, p. 426.

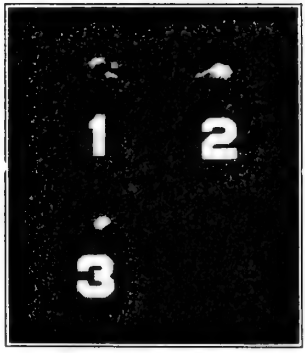
[3] Keible and Mall, "Human Embryology," Vol. I, p. 526.



1

DIAGRAM SHOWING HERNIAL OPENING IN DIAPHRAGM AND PERICARDIUM THROUGH WHICH PROTRUDED OMENTUM, LIVER, AND GALL-BLADDER. The right heart was deeply grooved by the liver lobes which had compressed it during growth.

2



3

MUSCLE THINNED OUT, LEAVING DELICATE EDGE OF TISSUE FORMING PART OF BORDER OF HERNIAL OPENING IN DIAPHRAGM. Microscopical findings of remaining border: "Edge of *diaphragmatic opening* appears well rounded and is covered by endothelium, evidently a congenital defect."

CALCULI FROM KIDNEYS AND URETER OF DOG WITH TRANSPLANTED URETER: (1) From right pelvis. (2) From left pelvis. (3) From right ureter. (¼ actual size.)

has been made to reduce the inevitable resistance at the point of anastomosis to within the physiological limit for the necessarily impaired ureter. When this resistance is too great the first evidence of physiological strain appears as a dilatation of the cephalad ureter. This dilatation has been noted at varying dis-

tances from the kidney pelvis. Other factors being constant, it seems that the length of the hydroureter from the uretero-pelvic junction varies directly with the duration of the terminal overload.

63 (995)

The resistance to mechanical injury of the erythrocytes of different species.

By PEYTON ROUS and J. R. TURNER.

[*From the Laboratories of the Rockefeller Institute for Medical Research.*]

As the first step in an analysis of the conditions under which red cells will survive *in vitro*, we have studied the effects of handling them, as in washing. That this may entail injury is suggested by the work of Meltzer,[1] who noted that a few minutes' shaking of whole blood hastens considerably the disintegration of the erythrocytes.

Our experiments show that in citrated plasma the red cells of the dog, rabbit, sheep and man withstand well the handling incident to ordinary washing. They may be centrifugalized and suspended again and again without hemolysis. The case is entirely different when cells in salt solution are repeatedly washed and suspended. Except in the case of human cells this entails marked injury, which expresses itself either in an immediate slight hemolysis, or more often in a shortening of the time during which the cells remain intact.

The protective action of plasma, even when dilute, is well shown when washed cells are suspended in it and in isotonic salt solution, and shaken. Hemolysis occurs much sooner in the salt solution. The experiments have brought out striking differences in the fragility of the red cells of different species—and, to a less degree, of different individuals. Dog cells shaken in the salt solution undergo a marked and almost immediate hemolysis. Rabbit corpuscles are somewhat less sensitive, and sheep corpuscles even less so, while the red cells of man are markedly

[1] Meltzer, S. J., *Johns Hopkins Hosp. Bull.*, 1900, IX, 134.

resistant, though in their case, too, the protective action of plasma can be demonstrated.

The resistance of the red cells to mechanical injury has little if any relation to their resistance to hypotonic salt solution. For example, the corpuscles of the dog, though much more easily destroyed by shaking than those of the sheep, will withstand a hypotonic salt solution in which the laking of sheep cells is pronounced. With the bloods of different individuals of the same species a similar lack of parallelism in the two resistances has been noted.

64 (996)

The protection of fragile erythrocytes against mechanical injury.

By PEYTON ROUS and J. R. TURNER.

[*From the Laboratories of the Rockefeller Institute for Medical Research.*]

In the preceding paper the fact has been stated that erythrocytes handled in salt solution undergo an injury which does not take place when they are in plasma. This has suggested tests of various substances for a protective action. We have found that the addition to Ringer's solution of gelatin in very small quantity —$\frac{1}{8}$ of 1 per cent.—protects the red cells completely, and that their prolonged sojourn in it is no more harmful than in plain Ringer's. Dog corpuscles which break down almost at once when shaken in Ringer's solution, resist prolonged shaking when in the gelatin-Ringer's. Corpuscles of the dog, rabbit and sheep, washed in this fluid and placed in ordinary Ringer's, remain intact much longer than when washed in the latter. Dog erythrocytes may keep several days, whereas when washed in plain Ringer's solution they break down within a few hours. Only in the case of human red cells does the protection afforded by gelatin seem unnecessary during washing. These cells last quite as well when handled in plain Ringer's.

That the erythrocytes of certain species differ markedly as regards the time they remain intact when washed and placed in isotonic salt solution, is well known. The experiments with the

gelatin-Ringer's solution show that this is due for the most part to differences in the fragility of the erythrocytes. Corpuscles of the several species in question, protected with gelatin during washing and placed in plain Ringer's, differ relatively little in their period of survival.

65 (997)

Experimentally fused embryos with special reference to giant larvæ formation, changes of symmetry, and changes of synchrony.

By **A. J. GOLDFARB.**

[*From the College of the City of New York.*]

Experimentally fused groups of two or more eggs of the sea-urchin *Arbacia punctulata* were studied individually from the blastula stage through the larval stage as late as the 14-day larvae. These isolated groups were studied with respect to the behavior of the three major tissues, body wall, gut and skeleton, and, of the processes taking place I wish to mention briefly only three.

1. Contrary to the views of Boveri and DeHaan two fused eggs may develop into a single giant larva even when the axes and symmetry of the two eggs or blastula or gastrula are not in the position of two blastomeres of an egg. A considerable number of fused pairs of eggs were followed through their entire development, in which the axes of the two numbers diverged 35 to 135 degrees from each other, yet these eggs gave rise to single giant larvæ.

Some of the processes involved in the transformation of two asymmetrically fused eggs include (1) change of symmetry, (2) retardation, (3) repression of one of the members, (4) absorption of one or more parts, (5) conflict of the skeleton centers, (6) size and rate factors in development.

2. There is a definite tendency for the two members to grow unequally, the one becoming increasingly small, though the rate of development is little or not affected. The law of synchrony as developed by recent investigators certainly does not apply in these grafts, and the regulative changes are due in largest part to the other factors enumerated.

3. Much evidence was collected that an absolute and relative change of axes takes place in many instances and in two directions, towards a symmetrical arrangement of the two members and, away from such symmetry, and the extent of such changes was determined and measured. There is no clear evidence of any change in polarity.

66 (998)

The influence of certain agents on the activity of phospho-nuclease.

By OLAF BERGEIM.

[*From the Laboratory of Physiological Chemistry of Jefferson Medical College.*]

The influence of certain chemical agents on the action of the phospho-nuclease of the intestinal mucosa of the hog was studied. In most cases 2 per cent. solutions of the substances tested were used with 10 c.c. of a 20 per cent. tissue extract, and 5 c.c. of 2 per cent. solution of neutral sodium nucleate.

Salts of Ca, Ba, Sr, and Li inhibited the action considerably while Mg, the phosphate of which is more soluble, did not inhibit. Uranium salts entirely inhibited. The inhibition in these cases appears to be due mainly to the removal of phosphate. The salts of the heavy metals, Hg, Ag, Cu, and U almost entirely inhibited while lead salts had less effect. The effect of these latter may be largely due to destruction of the enzyme.

Oxalate, tartrate, and fluoride had marked inhibitory effect while citrate did not show this. With the exception of citrate these form insoluble salts with Ca. Apparently the inhibitory action is due to removal of Ca ions. The suggestion that a slightly acid solution was favorable could not be confirmed. HCl to make 0.05 per cent. solution practically stopped the action while an equal amount of NaOH doubled the amount of phosphoric acid set free. The same favorable effect was found when a little $NaHCO_3$ was added and the mixture saturated with CO_2. Apparently a slightly alkaline or balancing solution is favorable. NaCl, K_2SO_4 and KI stimulated slightly. NH_4NO_3 and potassium arsenite inhibit somewhat. KCN in .25 per cent. neutral solution

paralyzed the action. In all of these cases the protective action of the protein of the intestinal extract must be borne in mind.

The inhibition by Ca precipitants may aid in explaining the toxicity of these agents for nucleated cells. The fact that while small amounts of Ca seem to be necessary for the action, larger amounts inhibit is of interest in connection with Ca metabolism. Nor can we disregard the fact that many of these substances (oxalate, tartrate, fluoride, uranium salts) produce a tubular nephritis in animals. It would appear that this was associated with a disturbed nuclein metabolism of the epithelial cells, and through this of the secretion of Ca and P, and as other evidence would indicate, of sugar and uric acid also; so that the excretion of Ca for example should be a good index of this function. This view is intimately bound up with the regulation of the blood reaction through phosphate excretion, and probably also to the related secretion of CO_2 by the lungs, which, as well as the kidneys, are high in phospho-nuclease. The intertransformation of Ca carbonate and phosphate in the bodies of higher and lower animals is a striking phenomenon in this connection.

67 (999)

Studies on so-called protective ferments. VI. On the action of anesthesia in anaphylaxis.

By **J. BRONFENBRENNER** and **M. J. SCHLESINGER.**

[*From the Pathological and Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pa.*]

It is assumed by Besredka,[1] that the shock in anaphylaxis is due to the direct toxic action of protein split products upon the cells of the central nervous system. Such a view of shock would most satisfactorily explain why anesthesia prevents the shock. The experiments of different authors however have definitely shown that the central nervous system is not primarily, but only secondarily involved in the anaphylactic symptom-complex. They failed however to explain the action of certain anesthetics as preventing shock.

[1] *C. R. Soc. Biol.*, 1907, T. 62.

In studying this question we found that certain anesthetics increase the antitryptic action of the blood sometimes as high as 100 per cent. and more. Although there might be some other relation, this increase of antitrypsin in the blood alone is sufficient to stop the activity of proteolytic enzyme and thus to avert the shock. As the animal recovers, the amount of antitrypsin is gradually coming down to normal and accordingly proteolytic enzyme is able to exert its action only in part, thus extending the process in duration at the expense of severity.

68 (1000)

The experimental plant of the New York State Commission on Ventilation.

By C.-E. A. WINSLOW.

[*From the New York State Commission on Ventilation.*]

The physiological investigations of the last twenty years have indicated that the ordinarily observed results produced by the air of crowded unventilated rooms are due to thermal rather than chemical conditions, high room temperatures producing serious physiological derangements, while the chemical constituents of the air of such rooms appear not to exert any measurable effects. For the further study of the reactions of the body to moderately high room temperatures, and for a more exhaustive investigation of possibly undetected chemical influences, the New York State Commission on Ventilation has equipped an experimental plant in rooms courteously placed at its disposal by the trustees of the College of the City of New York.

Since the effects to be observed would naturally be slight, it was necessary to provide a plant on a large enough scale for the observation of a number of subjects over considerable periods of time. On the other hand, since we were dealing not with calorimeter experiments but merely with the effects of ordinary atmospheric conditions upon the human body, it was not essential that these atmospheric conditions should be regulated within closer limits than those attainable under the best practical conditions.

The observation room of the plant is ten feet by fourteen feet

and ten feet high and is insulated with two inches of cork board and a half inch coating of cement with a smooth white cement finish. A skylight at the top is fitted with three sashes and the room is entered through three doors with air chambers between. The subjects may be observed from the apparatus room through a window. Air may be supplied to the observation room through one or more of four 12-inch openings in a 12 x 18 inch vertical duct and may be exhausted from a similar duct at the other end of the same side of the room. The air flow is measured at the inlet by a meter specially designed for the purpose. For maintaining desired temperature and humidity conditions without fresh air supply, the observation room is equipped with ammonia cooling coils, steam radiators and a humidifying pan. Desk fans are provided for securing local air circulation. Continuous records of temperature and humidity in the observation room are made by means of a Bristol recording psychrometer and samples of air for carbon dioxide determinations are collected by continuous aspiration through a wash bottle of sulphuric acid.

The apparatus room (11½ x 14 feet by 11 feet high) contains two 8 x 9 inch multivane fans for supply and exhaust and insulated ducts by means of which air is drawn in from above the roof and delivered either to the observation room or the apparatus room itself. Air may also be recirculated continuously through the observation room. The volume of air may be varied between 30 and 350 cubic feet per minute. The main duct is provided with tempering and reheating coils, and with a Warren Webster air washer for humidification and a drying tank containing trays of calcium chloride. The apparatus is fitted at all essential points with automatic apparatus for temperature and humidity control. It has, however, always been found necessary to supplement the automatic regulation by manual control. The apparatus room also contains animal cages surrounded by revolving glass boxes for exposing animals to the effect of dust-laden air.

The ammonia coils in the observation room are served by a four ton Brunswick Refrigerating Co. compressor with appurtenances.

The plant was designed to maintain conditions varying from those existing out of doors or less up to 100° F. in zero weather, with

humidities varying from the saturation point to practically nothing. With the exception of the reduction of humidity in warm weather, which the calcium chloride tank does not satisfactorily accomplish, the plant has fulfilled all our requirements. The extreme range in temperature during the day is usually 2° and very rarely over 4° and the extreme range in relative humidity ranges between two and ten per cent. of saturation. The carbon dioxide remains usually below 8 parts per 10,000 when air is supplied and when stagnant conditions are maintained it rises to between 30 and 90 parts depending on the number of occupants in the room and the weather conditions outside which influence inevitable leakage.

69 (1001)

The experimental methods of the New York State Commission on Ventilation.

By **Frederic S. Lee.**

[*From the New York State Commission on Ventilation.*]

Since December 8, 1913, the New York State Commission on Ventilation has been conducting an extended series of experiments on the physiological and psychological action of various atmospheric conditions. For most of the tests human beings have served as subjects; a few lines of observation have been carried out on animals. The rate of the heart beat and the blood pressure have been studied by the usual methods and have subsequently been evaluated according to the Crampton, the Barach and other indices. Bodily temperature has been measured chiefly by clinical thermometers and at times by the constant temperature recorder of Leeds and Northrup. This instrument consists of a self-balancing Wheatstone bridge, is sensitive to one tenth of a degree, and makes on paper a continuous record of rectal temperature. The apparatus proved very prone to get out of order and for this reason could not be used as constantly as was desired. Muscular work was performed by the lifting of dumb-bells to a given height, the number of lifts being recorded by a telephone counter. For more exact determinations of the amount of work performed a Krogh bicycle ergometer was employed and proved very satisfactory.

Respiration was studied by determining its rate and the volume of air respired, the carbon dioxide tension of the alveolar air by the Haldane method, and the volume of the dead space by the method of Douglas and Haldane, while the acidity of the blood was tested by means of both the carbon dioxide tension of the alveolar air and the dissociation curve of the hemoglobin by the method of Barcroft. By the usual methods determinations were made of the respiratory quotient, the amounts of carbohydrate and protein metabolism, the production of heat, and the specific gravity and freezing-point of the urine. Some determinations of the sensitivity of the skin were made by the method devised by Martin.

Appetite was studied by measurements of the number of calories represented in the food actually eaten by each subject from standard luncheons which were served in the observation room. The amount and the quality of mental work which each subject was capable of performing under the different atmospheric conditions were determined by means of a considerable variety of mental tests, such as the naming of colors and their opposites, the cancellation of given letters in a large group, the addition of numbers, mental multiplication, typewriting, the grading according to a given scale of specimens of handwriting, poetry, and English prose composition.

The action of the different atmospheric conditions upon the nasal mucous membrane was observed by means of rhinoscopic observations of the membrane, which were supplemented by the use of the Zwaardemaker plate. The significance of dust in the air in relation to infection was studied by exposing animals for stated periods to air containing dust from various sources, such as metal, hair, coal and mother-of-pearl, and subsequently inoculating the animals with the bacilli of tuberculosis. By means of an apparatus specially devised the amount of dust in the air under different conditions has been determined. The relation of atmospheric conditions to immunity has been studied by determinations of the agglutinins in the blood.

ABSTRACTS OF THE COMMUNICATIONS, PACIFIC COAST BRANCH.

Seventh meeting.

70 (1002)

Concentration of the protective bodies in anti-pneumococcus serum by means of specific precipitation.

By FREDERICK P. GAY, M.D., and HENRY T. CHICKERING, M.D.

[*From the Hospital of the Rockefeller Institute of Medical Research.*]

The addition of a water-clear extract of pneumococcus to the homologous antiserum produces a voluminous precipitate which carries down with it the agglutinins and practically the totality of the protective bodies against pneumococcus infection in animals. This precipitate when washed and resuspended in saline solution to the original volume of serum protects as well as the whole serum. The protein content of such solutions has varied from 0.09 to 0.34 per cent. as contrasted with about 6 per cent. in the original serum. The solution of this precipitate is not necessary to insure protection, and when produced by dilute alkali (NaOH) frequently destroys the immune bodies.

This concentration of the immune bodies differs from the method described by Dehne and Hamburger[1] for fixing tetanus antitoxin by means of antihorse serum and similar results with diphtheria antitoxin described by Weill,—Halle and Lemaire[2] in that the immune serum serves as a precipitin and not as precipitogen. By this reversal of reaction a corresponding reversal of dosage is possible which renders the method practical for concentrating the immune bodies for possible therapeutic use. An additional advantage of this method over concentration by chemical precipitation is that it can be rapidly and aseptically prepared and has a much lower protein content.

[1] Dehne and Hamburger, "Experimental Untersuchungen über die Folgen parenteralen Einverleibung von Pferdeserum," *Wein. Klin. Wochens.*, 1904, XVII, 807.

[2] Weill, Halle and Lemaire, (1) "Les Conditions de persistance de l'Immunite passive antidipterique. Ses relations avec la presence du serum antitoxique dans le sang et avec l'apparition de precipitine;" (2) "Antitoxine et Precipitine," *Comptes rend. de Soc. de Biol.*, 1906, LXI, 114, 407.

SCIENTIFIC PROCEEDINGS.

Abstracts of Communications.

Sixty-sixth Meeting.

Pathological Laboratory, Bellevue Hospital, March 17, 1915.

President Lusk in the chair.

71 (1003)

Tissue juice as a hemostatic.

By **Alfred F. Hess.**

[*From the Research Laboratory, Board of Health, New York City.*]

A very potent hemostatic can be prepared by extracting various tissues with salt solution. The most suitable in this regard is the brain, and somewhat less efficacious, liver or muscle tissue. Thromboplastic substance obtained in this way has very marked power when added to oxalated plasma or to blood, bringing about a clot with almost explosive rapidity. It can be maintained in a sterile condition by means of the addition of 0.3 per cent. tricresol, and in this state has been found to maintain its efficacy for at least a month. This preparation when tested locally upon animals, markedly diminishes the bleeding. In true hemophilia of man, which is characterized by delayed clotting of the blood, in two cases it checked the bleeding when applied locally after numerous other procedures had failed. It seems to be especially adapted for use in such cases.

When given intravenously to animals, it causes a shortening of the coagulation time. The blood when caught into the usual amount of 1 per cent. oxalate solution, does not remain fluid. A 2 per cent. solution of this preparation has been injected intravenously into human beings and found to decrease the clotting time.

72 (1004)

Comparison of certain properties of pancreatic and malt amylase preparations.

By **H. C. SHERMAN** and **M. D. SCHLESINGER.**

[*From the Laboratory of Food Chemistry, Columbia University.*]

The amylase preparations made from pancreas and from malt are similar in many respects but are not identical substances.

Both are essentially protein materials, showing typical reactions in the Millon, xanthoproteic, tryptophan and biuret tests, containing 15 to 16 per cent. of nitrogen, and yielding the different types of amino acids distinguishable by the Van Slyke method in proportions similar to those found in typical proteins by Dr. Van Slyke.

Both the pancreatic and the malt amylase preparations when heated in solution yield coagulated albumin and a proteose or peptone.

These and other observations are in harmony with Osborne's theory of the chemical nature of the enzyme, and not with the findings of Frankel and Hamburg or of Pribram.

Malt amylase is most active in a somewhat acid solution (P_H^+ 4.4 ± 0.2) whereas the optimum for pancreatic amylase is slightly alkaline.

Among the best preparations obtained in a long series of purification experiments the pancreatic is more than twice as active as the malt amylase. In 30 minutes at 40° the former produced 10,000 times, the latter 4,000 times, its weight of maltose. When allowed to act at the same temperature until no further action could be observed the pancreatic amylase preparation digested 2,000,000 times its weight of starch and produced 1,200,000 times its weight of maltose.

The most highly purified pancreatic amylase preparations show also a pronounced proteolytic action, while the corresponding malt amylase preparations show no proteolytic activity.

The results of the investigation are being published in a series of papers in the *Journal of the American Chemical Society.*

73 (1005)

The blood ptosis test and its use in experimental work in hygiene.

By C. WARD CRAMPTON.

[*From the Department of Education, New York City, Bureau of Educational Hygiene.*]

The modern health campaign has three parts.

1. The cure of disease,
2. The direct prevention of disease by sanitation, quarantine, instruction in hygiene, and the like, and
3. Euthenics.

This last includes physical training, play, and all measures calculated to increase resistance to disease and bodily efficiency.

The success of health and vitality increasing measures is difficult to estimate on account of the lack of tests. It is possible to measure the result of long-continued activities such as physical training, gymnastics, play, athletics, and good ventilation on the one hand, and fatigue-producing activities, such as school life of various kinds, on the other hand, by noting the increase or decrease of incidence of disease, and absence from school, and the percentage of hemoglobin, etc. These tests are difficult to control because they take a long time, and other factors cannot always be successfully eliminated or controlled. It is highly desirable to obtain some test of some important body function which will show clearly and rapidly by its variations, the beneficial or depressive effect of various conditions supposed to affect health. Such a test will be useful in proportion to the importance of the function tested and its accuracy in recording the variations of this function.

The following test promises to fulfill these conditions. It is well known that the splanchnic veins are very capacious, and if vaso-tone is relaxed, they fill at the expense of the rest of the body. The vaso control of the splanchnic area is in man, comparatively recently adjusted to the erect position. As such, it is easily wearied and easily damaged by unhygienic influences which decrease the efficiency of the sympathetic nervous system. The efficiency of this control is, I believe, measured by placing the

subject in a horizontal position and taking the systolic pressure in the brachial artery. The subject is then required to stand, and without removing the cuff, blood pressure is taken in a vertical position. In a perfectly strong and vigorous subject the splanchnic vaso-tone will increase and the blood pressure will be found raised about 10 millimeters of mercury. In an individual weakened by dissipation, overwork, lack of sleep, or by the incidence of disease, the blood pressure will tend not to rise but to fall. Under conditions which may still be classed as normal, this fall of pressure may amount to ten millimeters. These facts have been verified by repeated tests upon those known to be in good and in bad condition, in subjects well rested, and others thoroughly wearied. It appeared, therefore, at this point in the investigation, that we have arrived at a test of an important function and that the test could be expressed numerically on a scale ranging from plus ten to minus ten. A further factor of importance was, however, present. It was found in the vigorous subjects that the heart rate did not increase on standing, and in the wearied subjects it increases as much as forty-four beats per minute. It was further found that this difference varied with the blood pressure differences and in some cases took the place of the blood pressure variation. In other words, the same subject under the same conditions would show a weakness sometimes by a decrease in blood pressure, and at other times by an increase in heart rate, and vice versa. After further observation, it was determined that a decrease of one millimeter of mercury had a value of an increase in heart rate of approximately two. It was obviously necessary to consider both elements and to adjust the heart-rate changes with the corresponding blood-pressure changes. To do this, it was assumed that the total observed ranges in heart rate and blood pressure were equal in total value, and equal in each step in the scale in a proportion to approximately two to one. A table which balanced these two elements was constructed as shown on page 121.

The 100 per cent. rating indicates a rise of ten in pressure with practically no increase in the heart rate. Throughout the table, an inefficiency exhibited either in blood pressure or in heart rate is given a corresponding lower rating until zero is reached. The

zero point indicates approximately the condition in which the vaso-tone system is working so poorly that the subject cannot maintain an erect position. This test has been used by many observers to determine the condition of athletes and has been verified by putting the athlete through a test in running, etc., to check up the findings of the test. The results have as a rule verified the observed percentages. This test forms part of the

PERCENTAGE SCALE.

VASOMOTOR TONE.

Blood Pressure.

Heart Rate Increase.	Increase.					0	Decrease.				
	+10	+8	+6	+4	+2		−2	−4	−6	−8	−10
0 to 4	100	95	90	85	80	75	70	65	60	55	50
5 to 8	95	90	85	80	75	70	65	60	55	50	45
9 to 12	90	85	80	75	70	65	60	55	50	45	40
13 to 16	85	80	75	70	65	60	55	50	45	40	35
17 to 20	80	75	70	65	60	55	50	45	40	35	30
21 to 24	75	70	65	60	55	50	45	40	35	30	25
25 to 28	70	65	60	55	50	45	40	35	30	25	20
29 to 32	65	60	55	50	45	40	35	30	25	20	15
33 to 36	60	55	50	45	40	35	30	25	20	15	10
37 to 40	55	50	45	40	35	30	25	20	15	10	5
41 to 44	50	45	40	35	30	25	20	15	10	5	0

Note: In case of increase in pressure higher than + 10 add 5 per cent. to the + 10 column for each 2 millimeters in excess of 10.

routine examination in many colleges where athletes are examined by the physical director previous to certification of physical fitness. In five cases with five different observers, an athlete has presented himself for certification claiming to be in perfect condition and pointing to previous successful performances. In these cases the vaso-tone percentage was found very low and the candidate was referred for another examination on the next day. In these cases the candidates did not appear and were found to be ill. Thus it appeared that the test revealed a damaged vaso-tone, before subjective or objective symptoms were apparent. This test has been used to catalogue the effect of various school tasks upon the splanchnic vaso-tone. This test is being used by the New York State Commission on Ventilation to determine the effect of high and low temperature and humidities. In a pre-

liminary report, it was found that vaso-tone efficiency was 50 per cent. greater at 68° than at 86°. It is believed that this test will measure with reasonable accuracy the efficiency of the splanchnic vaso-tone and that this is an important indication of the efficiency of a body and related closely to vitality. It is realized that the test does not measure other important factors of physical and mental efficiency, and will not, for instance, reveal the structural condition of the heart. It does, however, open a new field for the measurement of the results of work calculated to improve physical condition.

74 (1006)

On the preservation in vitro of living erythrocytes.

By PEYTON ROUS, M.D. and J. R. TURNER, M.D.

[*From the Laboratories of the Rockefeller Institute for Medical Research.*]

The length of life of the functioning red blood cell is not known, but there is indirect evidence that it is several weeks at least. *A priori* one might suppose that if these elements were kept in the cold outside the body their period of survival would be much longer. But as a matter of fact in citrated plasma or defibrinated blood the erythrocytes of many species begin to break down within a week or ten days; and washed erythrocytes in normal salt solution or Ringer's fluid do not last even so long.

In previous papers we have shown that the early hemolysis of washed erythrocytes is attributable in large part to injury during washing; and that this injury can be prevented by the presence of a very little gelatin in the wash fluid (1/8th of 1 per cent.). But even when protected during washing the erythrocytes do not remain intact *in vitro* nearly so long as they are supposed to in the circulation. We have addressed ourselves to the problem of their preservation.

For reasons which need not here be entered into, our first experiments were made with solutions of inorganic salts to which non-protein colloids were added. But it was found that though gelatin will protect red cells against injury during washing it has

no preservative effect; agar proved toxic, as shown by early laking; and dextrin had only slight preservative qualities, except in concentrations which caused a browning of the blood pigment, presumably to methemoglobin. Soluble starch, the watery extract of coagulated blood serum, beef albumen, an aqueous solution of the alcohol-soluble constituents of blood serum, and even serum water made up to isotonicity with sodium chloride were all non-preservative. The sugars alone have proved well suited to our purpose. In a dextrose-Ringer's mixture containing 2½ per cent. of dextrose the erythrocytes of the sheep have been kept intact for a period of two months; and those of man for a month in a somewhat similar solution. The limits of the method have not yet been reached. The sugars which have proved best are saccharose and glucose. Isotonic mixtures are better than hypertonic. For the blood of each species a different preservative solution is required. Thus, the blood of the dog keeps best in a sugar-Ringer's-dextrin mixture, whereas for other bloods dextrin is useless if not harmful. It is interesting that though sugars and dextrin are *preservative* they are not *protective;* red cells handled in solutions of them undergo as much injury as in ordinary Ringer's.

Are the cells kept intact in the preservative mixtures to be considered as surviving? They can be washed repeatedly; will take up and give off oxygen; and those of the sheep when used for the Wassermann reaction behave exactly as do the freshly drawn cells of the same animal. But this is not sufficient evidence of viability. To determine the matter bleedings followed by transfusions have been performed, the blood of a number of animals being replaced so far as possible with red cells preserved for many days *in vitro* and suspended in salt solution. The results of such experiments with rabbits show that the washed and preserved blood cells remain alive. Following a disturbance in the blood count in the first few hours, associated with the replacement of more than half the total blood and due to discrepancy between the number of red cells taken out and that put in, to readjustment of the blood volume, etc., there is practically no change in the count, or in the readings of hemoglobin. Bile has never been found in the urine after the transfusions, nor hemo-

globin with any certainty. The guaiac test is sometimes faintly positive after the first twenty-four hours but so it sometimes is in control rabbits bled and injected with Ringer's solution, and at times even in normal rabbits. There is no rise in temperature and immediately after the operation the transfused animals are lively and seem quite normal. Control rabbits in which the blood is replaced by Ringer's solution recover very slowly from the profound anaemia. Animals of which the blood is replaced by blood collected and kept in Ringer's citrate may show severe disturbance associated with hemoglobin in the urine. And an animal transfused with blood kept in Ringer's solution had intense hemoglobinuria and died in convulsions. There is no doubt that washed erythrocytes left in a sugar-Ringer's mixture are really preserved alive, and preserved better than in plain Ringer's or in plasma-Ringer's-citrate.[1]

Weil has kept guinea-pig blood and dog blood several days in plasma with a minimum of citrate and then revived exsanguinated animals with it.[2] Do red cells survive longer in the preservative solutions we have devised than in such plasma citrate? There is no doubt that human cells and sheep cells do. In plasma-citrate these rapidly disintegrate. Rabbit's cells last longer but in their case we have had better results with the preservatives than with a plasma-Ringer's-citrate. On the other hand, it is possible that an optimum plasma-citrate medium has not yet been found. Our most recent experiments demonstrate that the blood of some species when allowed to flow directly into a large excess of a preservative fluid in which citrate is present can be kept for long periods. And since the cells soon settle out, and practically all the preserving fluid can be pipetted off previous to the employment of the blood for injection this constitutes a great simplification of method.

[1] Locke used one tenth of one per cent. of dextrose in the solution which bears his name. This amount of sugar is far too little for any preservative effect on the red blood cell.

[2] R. Weil, *Jour. Am. Med. Assn.*, 1915, LXIV, 425.

75 (1007)

The respiratory quotient in diabetes.

By GRAHAM LUSK.

[*From the Physiological Laboratory of the Cornell University Medical College, New York City.*]

Oxidation of protein in the body really consists in the destruction of a great variety of amino-acids. When glucose arises from protein in diabetes the oxidation is different from the normal. When the D : N ratio is 3.65 the respiratory quotient for protein falls from 0.801 to 0.634. From Osborne's analyses of meat protein, recalculated on the basis of Osborne's own determination of the deficiency of the analytical methods employed, it may be calculated that the six sugar-forming amino-acids, glycocoll, alaninē, aspartic acid, glutamic acid, proline and arginine, are present to the amount of 64.5 grams in 100 grams of meat protein. From the work of Ringer and Lusk and of Dakin and Dudley, it may be estimated that 44.4 grams of glucose arise from the several quantities of these amino-acids contained in 100 grams of meat. This would indicate a D : N of 2.75 and would explain the origin of 76 per cent. of the maximal sugar production from protein.

The estimated quantity of 64.5 grams of sugar-forming amino-acids would yield a respiratory quotient of 0.915 when oxidized normally, but if 44.4 grams of glucose be produced from them the respiratory quotient sinks to 0.675.

If one subtracts the influence of these sugar-forming amino-acids and the influence of the 1.07 grams of protein ammonia from the normal respiratory exchange, one may calculate that the respiratory quotient which represents the oxidation of the non-sugar-forming amino-acids is 0.716.

If one turns to Osborne's analyses it is found that the non-sugar-forming amino-acids consist in larger part (20 grams) of leucine, lysine and valine with respiratory quotients of 0.73, 0.71, 0.75 and in lesser quantity (7 grams) of histidine, phenyl-alanine and tyrosine with quotients of 0.90, 0.87, 0.89. Using Osborne's uncorrected figures (for corrections for lysine are not

available) one may estimate that in 100 grams of meat there are 27.16 grams of these six non-sugar-producing acids which on normal oxidation yield a respiratory quotient of 0.765 instead of 0.716 which was calculated. The lack of exact correspondence shows the comparative crudeness of the methods involved. It must also be remembered that the quantities present in meat of cystine and especially of serine, both of which are sugar formers, are unknown.

76 (1008)

On a simple method of diagnosing pregnancy, based upon the presence of specific enzymes in the urine.

By **R. H. MALONE, M.D.**

[*From the Department of Pathology, McGill University, Montreal.*]

It has been clearly demonstrated by Abderhalden and the host of workers following in his footsteps, that protective enzymes are developed in the body as a result of the presence of a foreign protein in the blood stream, whether that protein be derived from placental tissue, or carcinoma in the body, or be introduced from without for experimental purposes.

These enzymes, proteolytic in nature, have been found in the serum: their function is to digest the foreign protein and split it into amino-acids, in which form it may properly circulate in the blood stream, and be absorbed by the cells.

While working with Dr. A. A. Bruère at the Royal Victoria Hospital, Montreal, on a method of performing the Abderhalden Cancer test without the use of dialyzing thimbles, it was observed that a serum which gave a strongly positive test after incubation for 20 hours, was negative on the following day. The suggestion was made that certain enzymes had dialyzed out, causing the further splitting of peptone and amino-acids into simpler bodies which would not give the Ninhydrin reaction. Theoretically one might now expect that an enzyme which is dialyzable through a parchment thimble would also pass through the kidney and be found in the urine.

It was at this stage that Professor Adami called my attention

to Kiutsi's work on urine diagnosis[1] in which this passage of specific enzymes through the kidney is made the basis of a widespread method for the diagnosis of disease.

Kiutsi's method is as follows:

"By filtering urin of a pregnant through animal charcoal, the urin is clarified and protein and peptone taken off, *i. e.*, let it be filtered through animal charcoal several times until Biuret reaction is no longer positive. Then 5 c.c. of so treated urin is put into a test tube. Into it 0.1 gr. of Kiutsi's placenta is added and the mixture is left for six hours or fourteen hours. After this the entire liquid is filtered through a filter paper into another test tube, and 2 c.c. of sodium hydroxid is added. After shaking the contents a little, the test tube is held by the left hand in a slanting position. With the right hand the copper sulphate solution is taken in 1 c.c. pipette. On letting the copper sulphate solution run down slowly by the inside of the tube, where two liquids meet, a brilliant purple color may be formed. Then the reaction is positive. But if no such coloration takes place, the reaction is negative."

Kiutsi claims to have "repeated this method hundred times, and never missed," and says "By this method the early pregnance, the early abortion and the extra-uterus pregnance could positively be detected, and its reliability put even myself to astonishment." He also states that he has been able to diagnose cancer, nephritis, tuberculosis of the lungs, renal glycosuria, and other diseases by this method, using the proper substrate in each case.

Kiutsi, while indicating the broad outlines of this method, is careful not to give any details regarding the preparation of his dried substrates, and has avoided pointing out the precautions which have to be taken to obtain uniform results. His paper is remarkable, and that not alone from the importance of the fundamental observation and the naïveté and quaintness of its diction. Undoubtedly the combination of the claim to have discovered a practically universal diagnostic method with what appears to be a purposeful silence regarding the finer but essential details of

[1] M. Kiutsi, "Kiutsi's Urindiagnosis by Means of 'Filtration Process.'" June 10, 1914. Printed by Bunyeido, Sapporo (Japan).

that method must create at first an unfavorable impression. Nevertheless the observations tallied so remarkably with our own, as to demand confirmation. The work, if correct, opens up such a large field for research that the writer sought to verify it by a similar series of experiments.

In the absence of any details as to the method of preparing the dry substrate, the following plan was adopted.

Two placentas were obtained, freed from blood by washing in saline solution, and then in running water, and treated according to Abderhalden's directions until the water in which the substrate had been boiled for five minutes gave no ninhydrin reaction.

One half of this substrate was placed in a sterile jar containing 50 per cent. glycerine in water, covered with toluol and kept in the ice-box; the other half was treated as follows:

It was minced finely, dried in the oven at 80° C. for 4 hours, and then over-night at 55° C. Next day it was ground to a fine powder in a sterile mortar and kept in a desiccator over calcium chloride for 3 days. The appearance of the substrate is that of a fine, dry, brown powder which can be kept in a closely stoppered bottle without fear of autolysis or bacterial action.

The use of animal charcoal as recorded by Kiutsi for the purpose of removing bodies giving a positive biuret reaction was found unsatisfactory. The method was slow and tedious, fresh filters of charcoal had to be employed for every sample of urine, and often the filtrate showed a purplish tint due to coloring matters absorbed from the charcoal. As a substitute method, shaking with kaolin was tried. Experiments were then conducted to determine

1. The amount of kaolin necessary to remove from the urine all bodies giving a positive biuret reaction.
2. The optimum amount of dry substrate to be employed.
3. The optimum incubation period.
4. The effect of the acidity or alkalinity of the urine on the reaction.
5. The effect of bacterial growth during the incubation of the urine to be tested.

As a result of these experiments the following method was devised, and has been found to be satisfactory.

A freshly passed specimen of urine from a pregnant woman is tested for albumin by the biuret test. If the test be positive 15 c.c. of urine are shaken with 0.3 gram of kaolin for 10 minutes on a mechanical shaker, filtered and tested again; the biuret test should now be negative. If it be still positive the process must be repeated. 10 c.c. of the biuret-negative urine are then neutralized with 1 per cent. acetic acid, or with 2 per cent. sodium carbonate solution, 0.2 gram of dried placenta added, and the whole well shaken. The shaking I find essential. 0.5 c.c. toluol is added to restrict bacterial growth. The mixture is incubated for 12 hours, filtered, and 5 c.c. tested by the biuret test. If negative the remaining 5 c.c. are left in contact with the substrate, incubated for 4 hours longer, and tested again.

Controls of the urine of the pregnant woman without substrate, of urine from a male with and without substrate, from a non-pregnant female with and without substrate, and of the substrate in 10 c.c. of distilled water, are set up and tested in the same way.

The urine of the pregnant female in contact with the substrate should give a positive biuret reaction: all the controls should give negative reactions. The color of a positive test varies from deep purple to lilac or rose in different cases. All blues and greens are negative.

Up to the present time 59 cases have been examined. Of these, 12 urines tested *before* the above technique had been fully developed, gave the following results: one male gave a negative reaction both with the blood serum and the urine; of the 11 pregnant females, only 2 gave a positive reaction with the urine although in every case the blood serum was positive. Since using the kaolin method, and adopting the precautions mentioned in the preceding paragraphs, the results have been very satisfactory.

Urines from 47 Cases Examined.

Pregnant females	29—all positive.
Males	6—all negative.
Non-pregnant females	9—8 negative, 1 positive (fibroids of uterus).
Ectopic gestation	3—all positive.

These positive results in pregnant females were gained in the main from urines of cases estimated as from the 28th to 36th

weeks of gestation. Two cases were at about the third month.

It is perhaps scarcely necessary to point out that, as compared with Abderhalden's delicate and complicated serum test for pregnancy, this method is both simple and expeditious.

77 (1009)

The influence of chenopodium on the circulation and respiration.

By WILLIAM SALANT and A. E. LIVINGSTON.

[*From the Pharmacological Laboratory, Bureau of Chemistry, U. S. Department of Agriculture, Washington, D. C.*]

The intravenous injection of one to two per cent. emulsions indicates that the oil of chenopodium is a circulatory, as well as a respiratory depressant. Blood pressure fell after a dose of 0.02 c.c. per kilo was introduced into rabbits, cats and dogs, but the absolute, as well as the relative effect, varied in different individuals. While large doses produced a greater fall of blood pressure this was not always in proportion to the size of the dose. The volume of the kidney followed closely the blood pressure, thus indicating that the effect on the latter is of cardiac origin. That chenopodium is a cardiac depressant was also shown in experiments on the isolated frog heart. A solution of 1 : 2,000, of chenopodium, or its active principle, ascaridole, perfused for one to two minutes, caused a marked decrease of force, as well as frequency of cardiac action which was not always observed, however, when the perfusion time was reduced to half a minute only. It was frequently absent after the initial perfusion and sometimes when this was repeated once or twice after suitable intervals, but depression of the heart was usually produced when a sufficient number of perfusions were made in each case. Cardiac irritability after vagus stimulation which was tested in dogs was found to be decreased after chenopodium.

The action of chenopodium on respiration varied in different animals, being less effective in rabbits than in cats or dogs. Small doses, about 0.02 c.c. per kilo may produce respiratory depression in all animals. In some experiments the effect was observed after

the initial dose, in others, however, only after the two or more doses were given. Larger doses, 0.04 to 0.08 c.c. per kilo, produced apnea in cats and dogs for a variable period, which was followed by very slow respiration.

78 (1010)

The absorption and elimination of chenopodium.

By WILLIAM SALANT and A. E. LIVINGSTON.

[*From the Pharmacological Laboratory, Bureau of Chemistry, U. S. Department of Agriculture, Washington, D. C.*]

The introduction of chenopodium into the stomach or small intestine of different animals after previously ligating the duodenum immediately below the pylorus was frequently followed by the appearance of symptoms of chenopodium poisoning.

In rabbits evidence of absorption from the stomach was obtained in some cases after 40 to 95 minutes. In others, however, several hours have elapsed without showing any effects. Absorption from the small intestine was particularly rapid in cats. When 2 to 5 c.c. of the oil was emulsified and introduced into the duodenum symptoms appeared in some individuals almost immediately after, in others there was a delay of five minutes. Absorption of chenopodium from the stomach also takes place in cats but the process is much slower. The effect of chenopodium poisoning was noticed one and three quarter hours after its introduction into the stomach in some experiments, but in other cases no evidence of absorption could be obtained during the lapse of this interval of time. Experiments on dogs indicate that the absorption of chenopodium is much slower in these animals than in cats.

When chenopodium was given intravenously its presence in the expired air could be easily detected. The odor was especially marked after large quantities were injected. The urine and bile showed no evidence of chenopodium.

79 (1011)

Demonstration in vitro of the specific affinity of thyroid cells for iodin.

By DAVID MARINE.

[*From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University, Cleveland.*]

It is a well-known fact that thyroid tissue in vivo has a specific affinity for iodin. This has been demonstrated in several ways. The simplest and most obvious means is afforded by taking advantage of the spontaneous active hyperplasia of dogs. Having shown that the per cent. of iodin in the gland varies inversely with the degree of active hyperplasia, we were able to demonstrate that the ability of the gland to take up iodin varies with the degree of active hyperplasia present; or if expressed from the viewpoint of chemistry, the ability of thyroid tissue in vivo to take up iodin varies inversely with the degree of saturation of the gland with iodin. Such relatively large proportions of a given intake of iodin may be stored by the thyroid (for example, the recovery of 4.5 mgm. I from a 7.2 gram thyroid lobe in a dog weighing 8 kilos from a total of 50 mgm. KI given by mouth in 10 days) in vivo that it seems likely the surviving thyroid cells in vitro would exhibit this same affinity, and if so it could readily be demonstrated by perfusion.

We have perfused a large series of spleens, kidneys and thyroids of dogs, using defibrinated blood containing ⅓ (by volume) of Ringer's solution. Iodin as KI was added to the perfusion fluid in amounts varying from 5 mgm. to 40 mgm. All perfusions were carried out at temperatures varying between 35° and 37° C. All the thyroid lobes used were goitrous, varying histologically from marked active hyperplasias to colloid goitres, and in weight from 11 to 81 grams. The perfusions were continued from 1 to 2 hours, and the glands washed with Ringer's for 20 minutes. Iodin and histological examinations were made both on the control and the perfused glands. It was found that relatively large amounts of the KI were held in the thyroid which could not be washed out

by the Ringer's solution, while with the spleen and kidney none was held. It was also noted that the amount of KI taken up by a thyroid does not depend on the amount (concentration) of KI in the perfusate. Relatively much less was taken up when 40 mgm. were added to a 75 c.c. perfusate than when 10 mgm. were used. The most interesting observation was that the more marked the hyperplasia (*i. e.*, the less iodin in the gland originally), the more iodin was taken up and also the more rapidly it was taken up, just as in the case of in vivo experiments.

Thus grouping the glands according to their anatomical structure, it was found that from 10 mgm. KI the marked hyperplasias increased their iodin contents over 1,000 per cent.; the moderate hyperplasias increased over 200 per cent.; the colloid early hyperplasias increased over 100 per cent.; and the pure colloid glands about 20 per cent. This is shown more in detail in the following tabulation:

Anatomical Condition of Gland.	No. of Cases.	Average Iodin* per Gm. Before Perfusion.	Average Iodin per Gm. After Perfusion.	Average Increase in Iodin per Gm.	Per Cent. Increase in Iodin.
Marked hyperplasia.....	5	0.07	0.79	0.72	1,000+
Moderate hyperplasia.....	3	0.23	0.77	0.54	200+
Colloid early hyperplasia....	3	0.47	1.14	0.67	100+
Colloid glands.....	3	1.03	1.23	0.20	19+

Thyroid glands undergo autolysis in a few hours after removal from the body especially if kept around the body temperature. This is recognized on microscopic examination by a desquamation of the alveolar epithelium. It was found that all such glands not only fail to take up iodin from the perfusate, but lose iodin to the perfusate, a finding that we interpret as meaning that the dead cells have lost the power of storing iodin, or that the taking up of iodin by the thyroid is a property of surviving cells. Studies to determine whether the iodin taken up is as active pharmacologically as the naturally iodized thyroglobulin have not been completed. However, since the amount of iodin taken up by a given perfused gland may be independent of its concentration in the perfusate, and since the amount taken up and the rapidity of its storage varies directly with the degree of active hyperplasia,

*Expressed in milligrams per gram of dried gland.

and since only anatomically intact glands exhibit this characteristic, and since kidneys and spleens perfused under similar conditions do not take up iodin, we believe one may conclude that the surviving thyroid cells in vitro exhibit the same specific biological affinity for iodin as is manifested by the thyroid cells in vivo.

80 (1012)

The clinical actions of veratrum.

By RUSSELL J. COLLINS and PAUL J. HANZLIK.

[*From the Pharmacological Laboratory, Medical School, Western Reserve University, Cleveland.*]

The object of this study was to ascertain more definitely the effects produced by veratrum in normal and diseased human individuals, with special reference to the circulatory system. Many of the studies reported in the literature lack definite objective data, and whatever data exist need the confirmation of the improved and more modern methods of observation. Pharmacologically, the effects of veratrum are well understood, and the drug is prompt and effective. On the other hand, the reported clinical results are contradictory, and the drug is variously reported as uncertain, ineffective or too "toxic." However, there is reason to believe that the circulatory effects obtained in patients may resemble the pharmacological and that veratrum might be useful as a therapeutic measure for certain circulatory conditions.

In all eight individuals were studied. Of these six were convalescent and their circulations were clinically judged to be about normal. Two were cases of hypertonus. The patients always rested in the horizontal position in bed on the days when the pulse rate and blood pressure were taken. The pulse was taken for half a minute at the time of the first dose of veratrum and at intervals of fifteen minutes until the effects of the drug were pronounced. The blood pressure was taken by the auscultatory method before the administration of the drug and again when the pulse rate had reached a minimum. Certain of the cases walked around when the pulse rate reached its minimum with no effect upon the rate. The preparation used was the 10 per cent. tincture

from *Veratrum album*. Each dose was given in one to three glasses of water, and usually no gastric irritation resulted. However, all patients complained of fullness and throbbing in the head when the pulse rate reached its minimum. The following conclusions appeared to be justified from the data thus far obtained.

1. The therapeutically effective dose of the tincture of veratrum album for adults ranges from 30 to 75 minims (administered in doses of 10 to 15 minims, an hour apart).

2. Clinically, the effects of veratrum resemble the pharmacological, and consist of a slowing of the pulse rate amounting to 12 to 42 beats per minute and a fall of systolic blood pressure amounting to about 39 mm.; of the diastolic 32 mm. The two hypertonus cases showed an average systolic fall of 49 mm.; of diastolic 8.5 mm.

3. The circulatory effects produced by veratrum take place independently of the "toxic" symptoms, such as nausea and vomiting.

81 (1013)

The effect of phlorhizin on tumors in animals.

By **F. C. WOOD** and **E. H. MCLEAN**.

[*From Columbia University, George Crocker Special Research Fund, F. C. Wood, Director.*]

In 1914 Benedict and Lewis[1] reported the cure of malignant tumors in rats by the induction of glycosuria by phlorhizin. During the past few months similar experiments have been carried on in the laboratory of the Crocker Fund, using the same tumor—Buffalo rat sarcoma—and a progressively growing, highly malignant mouse carcinoma. In addition, seven mice bearing spontaneous tumors have been treated. The treated animals were kept on a diet of meat and lard, as in the experiments of Benedict and Lewis. The rats received subcutaneously 0.003 gram phlorhizin in olive oil, and the mice 0.001 gram, at two or three day intervals; and the collected urines were examined frequently at the end of the second or third day after injection, and found to give positive Fehling reaction.

[1] PROC. SOC. EXPER. BIOL. AND MED., 1914, xi, 134.

Treatment was begun seventeen days after inoculation with the tumor, except in the cases of a few animals which were treated on the tenth day, and of a few which were first rendered diabetic and then inoculated. None of the tumors at the beginning of treatment had reached the size of the largest tumors reported cured by Benedict and Lewis.

Of the rats, there were alive twenty-four days after inoculation and seven days after beginning of treatment, 81 treated animals and 89 controls. Of the treated rats, 37 per cent. showed partial or subsequently complete absorption, while 58 per cent. of the controls had undergone spontaneous absorption. The largest tumor to disappear was among the controls and measured 26 × 14 mm. The largest growth noted occurred among the animals rendered diabetic before inoculation.

The laboratory stock of Buffalo rat sarcoma for the past fifteen months, representing over five hundred tumors, has showed 40 per cent. spontaneous absorption.

The mice with the transplantable carcinoma showed no cases of absorption, and those treated did not differ from the controls except in the death rate. The spontaneous tumors were not affected by the treatment.

In view of the great tendency of the Buffalo rat sarcoma to undergo spontaneous absorption and the failure of the treatment in progressively growing tumors, the results of Benedict and Lewis must be considered as due to spontaneous absorption rather than to the effect of induced diabetes.

82 (1014)

A new principle in isolation of spirochetes in pure culture.

By J. BRONFENBRENNER.

[*From the Pathological and Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pa.*]

In attempting to obtain pure cultures of spirochetes from the lesions of rabbits showing symptoms of generalized lues, I was confronted with extreme difficulties in the case of two strains

especially—one on the eyebrow of a rabbit infected by the intravenous inoculation of syphilitic blood and the other deriving from the condyloma on the vagina of a rabbit infected by coitus from a male rabbit having specific lesion on the prepuce. The bacterial contamination in each case was so abundant, that numerous attempts at purification using original Noguchi method failed for months. Having noticed earlier[1] that certain antiseptics in proper quantities exert a marked accelerating action upon the growth of spirochetes, I prepared media containing salvarsan in very small amounts and finally after 10 passages succeeded in isolating both strains of spirochetes, which apparently have remained pure for the last five months. In another series of experiments I tried to make use of the fact that anilin dyes, which exert marked sterilizing action on bacteria even in dilutions of 1:5,000 and 1 : 10,000, seem not to inhibit the growth of certain spirochetes in much greater concentrations.[2] The experiments in this direction are still not completed, as so far it was impossible to find a dye which would uniformly inhibit the growth of all the bacteria occurring in contaminated syphilitic material in a concentration which would allow the life of all the different strains of spirochetes.

83 (1015)

The demonstration of tryptic digestion by an activated serum.

By J. BRONFENBRENNER and K. M. SCOTT.

[*From the Pathological and Research Laboratories of the Western Pennsylvania Hospital, Pittsburgh, Pa.*]

In the earlier publications it was shown, that the placenta in the Abderhalden reaction is not digested.[3] It was assumed then that the dialyzable split products of protein appearing during the test originate from the serum as the result of its autodigestion.[4] It was shown also that although the normal serum shows no digestive power, such tryptic activity may be demonstrated in

[1] *Journal of Pharmacology and Exp. Therap.*, 1913, Vol. IV, p. 333.

[2] *Ibidem.*

[3] J. Bronfenbrenner, *J. of Exp. Med.*, 1915, Vol. XXI.

[4] J. Bronfenbrenner, PROC. SOC. EXP. BIOL. AND MED., 1914, Vol. XII, p. 7.

any fresh serum if it is rendered active by the removal of its antitrypsin.[1] In the recent experiments we have succeeded in demonstrating the proteolytic activity of the serum of pregnant individuals after the removal of its antitrypsin with boiled placenta, by allowing such a serum to act upon the standard suspension of fresh placenta cells. The number of cells were counted on a Fuchs-Rosenthal counting chamber at intervals during the experiment, and it was noticed that the cells underwent disintegration, only when mixed with the serum previously exhausted of its antitrypsin, whereas the control mixtures containing the whole male or female serum or salt solution remained practically unchanged. Such a digestion of placenta cells is not specific, as we have also observed it with the male serum, deprived of its antitrypsin by a non-specific mechanism, such as adsorption by kaolin or starch, as well as by the extraction with chloroform.

84 (1016)

The effect of adrenalin on the pupil after removal of the ciliary ganglion.

By DON R. JOSEPH.

[*From the Department of Physiology, St. Louis University.*]

Cats were used exclusively in these experiments. One ciliary ganglion was removed under ether anesthesia. The comparative irritability of the two irises to minimal doses of adrenalin was tested soon after the operation (1 to 4 hours) and again later (22 to 55 or more hours). In a few cases tests were made as long as 60 to 77 days after the operation. The adrenalin was injected into a saphenous vein. No ether was required.

Stated briefly the results are these: Removal of the ciliary ganglion renders the corresponding iris hypersensitive to adrenalin. Some increase in sensitiveness is occasionally seen within an hour after removal of the ciliary ganglion, but in most cases the maximal increase does not appear under 4 hours. The heightened irritability to adrenalin was still present after 60 to 77 days. The

[1] J. Bronfenbrenner, PROC. SOC. EXP. BIOL. AND MED., 1914, Vol. XII, p. 3. J. Bronfenbrenner, W. J. Mitchel and P. Titus (in press).

irritability of the gangliectomized iris was from 3 to 20 times as great as that of the normal iris. The adrenalin effect lasted definitely longer in the operated eye than in the normal. After the smallest doses used this difference was not great, but after the larger doses (*e. g.*, 1/50 c.c. 1 : 1,000 Parke Davis solution) it was marked—for example, the normal iris recovered completely within 10 to 20 seconds, while the iris deprived of its ciliary ganglion required from 3 to 4 minutes for recovery. Adrenalin produces, after removal of the ciliary ganglion, a dilatation of the pupil.

SCIENTIFIC PROCEEDINGS.

Abstracts of Communications.

Sixty-seventh meeting.

University and Bellevue Hospital Medical College, April 21, 1915.
President Lusk in the chair.

85 (1017)

The effect upon appetite of the chemical constituents of the air of occupied rooms.

By **C.-E. A. Winslow** and **G. T. Palmer.**

[*From the Laboratory of the New York State Commission on Ventilation.*]

It has been shown by many observers that the ordinary effects of the air of an unventilated occupied room are due to its high temperature rather than to its chemical composition. In the experiments carried out during the past two years by the New York State Commission on Ventilation, we have found that neither the pulse, blood pressure, body temperature, respiration nor metabolism are influenced to a measurable degree when human subjects are exposed for periods of from 4 to 7 hours to the air of a room in which all the chemical products due to human occupancy have been allowed to accumulate (so that the carbon dioxide averages over 30 parts per 10,000)—provided the temperature of the chamber be kept down by artificial means.

In the course of our investigation we have however, discovered a new measure of the influence of vitiated air which seems to indicate that there is after all an effect produced upon the body by the chemical constituents of the air of an occupied room. This effect is manifested in a diminished appetite for food.

The subjects in the first three of the five series of experiments reported which are tabulated below were young men, mostly

students at the College of the City of New York or at New York University, and in the last two series young women. For five days a week for a period of from two to six weeks, they were placed in the observation room of the experimental plant at the College of the City of New York (described *Proc. Soc. Exp. Biol.*, Vol. XII, p. 111). In each series of experiments the subjects were supplied with a fresh air supply of 45 cubic feet per minute on half the days while on the other days no air was supplied and (subject to unavoidable leakage through walls and ceiling) the carbon dioxide, organic matter, and whatever else was given off from mouths, bodies, and clothing accumulated in the room. Temperature and humidity however, were controlled so as to be the same on both ventilation and no-ventilation days. In the last three series of experiments, three desk fans were kept in motion at all times so as to prevent the introduction of an air movement factor by the current from the inlet duct on the ventilation days.

After the subjects had been in the room for from 2 to 3 hours, a luncheon made up of weighed portions of known calorific value, was served and the amount of food left uneaten was weighed to determine by difference the amount consumed. The diet was varied from day to day but with the exception of Series III was so arranged that each article of food appeared an equal number of times on the ventilation and no-ventilation days.

TABLE I.

Series.	Date.	No. of Subjects.	Sex.	No. of Days.	Hours in Chamber before Lunch.	Average CO_2 at End.		Average Calories Consumed.		Excess Favoring Ventil. Day.	
						Vent.	No Vent.	Vent.	No Vent.	Cal.	%
III.	June 8–July 27 '14	4	M	18	3–3½	7.5	29.5	1,308	1,151	157	13.6
VII.	Oct. 12–Nov. 6	4	M	20	3	9.0	50	1,620	1,492	128	8.6
X.	Dec. 8–Jan. 29 '15	7	M	28	2¼	9.5	36	2,057	1,971	86	4.4
XI.[1]	Feb. 1–19	8	F	12	2¼	7.0	37.5	1,313	1,381	—68	—4.9
XII.	Feb. 22–Mar. 19.	8	F	20	2¼	10.0	37.5	956	895	61	6.8

The carbon dioxide as indicated in the table above averaged between 29 and 50 parts on the no-ventilation days and there was usually a slight odor noticeable and sometimes a strong one.

In Series XII the opinions of the subject as to comfort were recorded and the average expression favored the no-ventilation condition.

[1] This series was vitiated by special conditions noted below.

In Series XI there was a slight excess of food consumed on the no-ventilation days. This series was however rendered practically valueless by the fact that after it was under way we discovered that religious dietary laws, observed but loosely at first, but gradually with more strictness, had prevented the use of certain articles of the diet. This influence was quite impossible to measure or to balance. The results however are included for completeness.

The other four series show a consistent excess of food consumption on the ventilation days. In view of the fact that these series represent averages of 71, 80, 196, and 160 meals respectively we believe them to be significant. In Series III and VII where the food left by each subject was separately weighed every one of the 8 different subjects ate more on the ventilation days.

The reliability of these figures based on the number of observations and their departure from the mean has been determined mathematically by Mr. W. A. McCall, psychologist on the staff of the Commission.

The chances that the differences in calories consumed between ventilation and no-ventilation days may be zero or may favor the other condition, are expressed in Table II.

TABLE II.

Series.	Chance of Different Result.	Interpretation.
III	0.38 chance in 100	Very reliable.
VII	1.0 " " "	Highly reliable.
X	9.0 " " "	Probable.
XI	18.0 " " "	"
XII	12.0 " " "	"

This effect on appetite of the absence of ventilation, though slight, is apparently a persistent one. At the beginning of an experiment there is but little difference noted on the two types of days. As the novelty of the environment and the meal wears off however, the effect of breathing the same air over and over again seems to exert an increasing influence. This action is illustrated in Series XII, where the average excess of food consumed on ventilation days was 6.8 per cent. During the first two weeks this excess was but 2.8 per cent. In the last two weeks it amounted to 10.8 per cent.

A separate computation of the bread and butter consumption at

each meal has been made and these results bear out the result for the entire meal as indicated in the table below. It was thought that this part of the meal might give a more exact measure of hunger, its attractiveness being less subject to variation than the meats and desserts.

TABLE III.

Series.	Per Cent. Excess Bread and Butter Eaten on Ventilation Days.
III.	5.2
VII.	5.7
X.	5.3
XI.	—2.2
XII.	6.1

These experiments seem to warrant the conclusion that there are substances present in the air of an unventilated occupied room (even when its temperature and humidity are controlled) which in some way, and without producing conscious discomfort or detectable physiological symptoms, diminish the appetite for food. The effect of such an influence might in time be very important and it seems possible that the observed beneficial effects of fresh air may to some extent be connected with this phenomenon.

86 (1018)

Protective inoculation against mumps.

By ALFRED F. HESS.

[*From the Research Laboratory, Board of Health, New York City.*]

In view of the fact that mumps confers a marked immunity on the person who has had the disease, that a second attack is rare, the blood of convalescents was used in a prophylactic way. Six to eight c.c. of blood was injected intramuscularly in 17 cases. These children were in wards where there had been cases of mumps for the past month and where it continued to appear for a month following these inoculations. In no case did one of the inoculated children develop mumps, whereas one third to one half of the non-inoculated cases developed the disease. The blood was taken from children who had just recovered or had been well for about ten days.

It would seem that this procedure could be made use of in the institution as well as in the home, and that this type of therapy could be adapted in the case of measles and other infectious diseases.

87 (1019)

A theory of internal disinfection with nascent formaldehyd.

By WILLIAM N. BERG.

[*From the Division of Pathology, Bureau of Animal Industry, Washington, D. C.*]

The works of a large number of investigators have shown that under ordinary conditions the cleavage of urotropin into its components, formaldehyd and ammonia, takes place only in the urinary tract and in other acid media. In the neutral tissue fluids this cleavage does not take place.

During their work on infectious abortion in cattle, Mohler and Traum[1] fed urotropin to cows for the purpose of ascertaining whether this substance would pass into the udder as formaldehyd as stated by Klein.[2] In a number of tests on 5 cows that received from 10 to 80 grams of urotropin per day, the milk contained urotropin but no formaldehyd.

In his studies on acid intoxication, Szili[3] found that the alkalinity of the blood of rabbits, dogs and sheep could be appreciably lowered by the intravenous injection of 0.6 per cent. hydrochloric acid. Insofar as the cleavage of urotropin in the urinary tract is probably brought about or assisted by the acid phosphates present it seemed reasonable to suppose that this cleavage might also be brought about in the neutral tissue fluids if the alkalinity of these fluids were slightly lowered by the administration of acid.

In the work now in progress, cows receive large doses of urotropin by mouth (up to 3 grams per kilo of body weight) followed immediately by the intravenous injection of several liters of 0.6 per cent. ($n/6$) or 0.9 per cent. ($n/4$) hydrochloric acid, in Ringer solution. Samples of milk are obtained and tested for formaldehyd.

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[1] Bureau of Animal Industry Circular 216.

[2] *Proc. Amer. Vet. Med. Asson.*, 1913, p. 395.

[3] *Arch. f. d. ges. Physiol.*, Bd. 115, p. 82, 1906.

The theory involved in this procedure is as follows: The urotropin in contact with acid or acid phosphate breaks up into formaldehyd and ammonia. The ammonia thus liberated is available for neutralizing the acid injected, so that an animal that has received urotropin should be more resistant to the harmful effects of the injected acid than one that has not received urotropin. In round numbers, 1 gram of urotropin will liberate 1 gram of formaldehyd and sufficient ammonia to neutralize 1 gram of hydrochloric acid.

The results obtained thus far are not conclusive. In a total of 10 experiments on 4 cows that received both acid and urotropin, (see accompanying table) formaldehyd was detected in the milk 4 times and was not detected 6 times. The positive findings are tentatively regarded as correct. In some cases, the amounts of hydrochloric acid that could be injected into cows without apparent injury, were so unexpectedly large, that the results are presented now because of their possible interest to those studying acidosis or the adaptibility of the vascular system.

Animal.	Date.	Body Weight, Kilos.	Injected Intravenously.		Urotropin Fed by Mouth, Grams.	Formaldehyd in Milk.	Grams HCl per Kilo Body Weight.
			Liters.	Per Cent. HCl.			
Cow 715	2/15	461	6	0.6	1,350	Absent	0.08
	2/17		13.5	0.6	1,350	Absent	0.18
Cow 1009 ...	3/13	250	15.5	0.6	None	No	0.37
	3/20	209	20	0.9	627	Milk	0.87 (after 48 hour fast)
Cow 1013 ...	1/15	293	11.5	0.6	80	Absent	0.23
	1/16		12	0.6	80	Absent	0.25
	1/27		20	0.9	907	Present?	0.61
	3/27	227	2.5	0.6	570	Absent	0.07 killed (had fasted 48 hours)
Cow 1026 ...	2/10	304	3	0.9	900	Present?	0.09 killed
Cow 1042 ...	1/20	231	12	0.9	80	Absent	0.47
	4/1	239	8.4	0.9	478	Trace	0.32 killed
Cow 1096....	2/1	391	4.4	0.9	None		0.10 killed
Steer 1128 ..	2/5	339	10	0.9	None		0.26
	3/17		31.7	0.6	None		0.56
	3/24	300	23	0.9	900		0.70 killed (had fasted 48 hours)
Cow 852.....	4/7	386	9.2	0.9	772	Present 1:100 000	0.22 killed

The animals varied greatly in their tolerance for the injected acid. Thus Cow 1026 was killed by a single injection of 3 liters

of 0.9 per cent. hydrochloric acid: Steer 1128 was killed by the third injection of 23 liters of 0.9 per cent. acid; while Cow 1009 still lives after receiving the unexpectedly large amount of 20 liters of 0.9 per cent. acid following an injection of 15.5 liters of 0.6 per cent. acid made seven days before. In Szili's work, the largest dose of acid tolerated by the experimental animal (a ram) was 0.23 gram of hydrochloric acid per kilo of body weight. In the present work, Cow 1009 is apparently in good condition after receiving 0.87 gram of hydrochloric acid per kilo of body weight.

88 (1020)

Anaphylaxis to formed or cellular elements.

By RICHARD WEIL and B. S. DENZER.

[*From the Department of Experimental Therapeutics, Cornell Medical School.*]

Our present knowledge of anaphylaxis is based almost entirely on the study of proteins in solution, such as blood serum. From the standpoint of infectious disease, the analysis of the immunological reaction to formed elements would appear to be of greater importance. The anaphylactic response to bacteria has regularly been found to be extremely slight. The present report deals with a study of the anaphylactic response to red blood cells.

Friedberger reported during the current year that guinea pigs could not be sensitized to alien red blood cells either by the active or by the passive method. On the contrary, these animals can regularly be sensitized by either method provided the proper technique be followed. In order to sensitize actively against alien red blood cells it is essential to give a series (2 or 3) of preliminary injections, instead of the single sensitizing injection which is customary in the case of serum. The reason for this will be obvious from the subsequent data. As regards passive sensitization, it is of importance to note that Friedberger, like Thiele and Embleton and others who have worked on this subject, used the serum of rabbits immunized against sheep red blood cells. This particular type of serum, however, is peculiarly unfitted for such an experiment. It possesses primary toxicity for the

guinea-pig tissues, which is usually ascribed to the presence of the same antigen in sheep cells and guinea-pigs cells. Consequently the latter neutralize the injected hemolysins, instead of anchoring them in unchanged form. If, however, the serum of rabbits immunized against ox red blood cells is used, passive sensitization is invariably induced.

The mechanism differs somewhat from that of serum anaphylaxis. As in the latter, indeed, the essential factor is the cellular or anchored antibody. In addition, however, there must be sufficient circulating antibody to break up the alien cell (hemolysin), dissolve its protein, and so bring it into intimate contact with the anchored antibody. It is on this account that an animal must be actually partially immunized, so that its blood gives a hemolytic titer, in order to sensitize it. These two factors have been demonstrated by showing that passively sensitized guinea-pigs which have then been thoroughly perfused with normal guinea-pig blood, are no longer sensitive to washed alien red cells, but do succumb to the injection of sensitized cells. Actively sensitized animals react in the same fashion, if the experiments are done at a long interval after primary sensitization, when circulating hemolysin has disappeared. Finally, in all animals dying of red cell anaphylaxis the blood serum is tinged with hemoglobin. As regards controls, it may be said that the injection of sensitized cells, or the simultaneous injection of cells and hemolytic serum has no effect.

89 (1021)

The origin of endogenous uric acid.

By **R. L. STEHLE.**

[*From the Laboratory of Physiological Chemistry, Sheffield Scientific School of Yale University.*]

The source of the endogenous uric acid of the urine has been the cause of much speculation and experimentation for years. The theories that it arises from glandular or muscular activity, however, have claimed most attention.

Experiments have been conducted on man to determine the

effect of activity of the alimentary apparatus upon the excretion of endogenous uric acid. To this end a comparison was made of the hourly uric acid excretion during a fasting condition and that when the digestive glands had been stimulated in various ways. The succagogues employed were pure nutrients—protein, fat and carbohydrate and combinations of these—pilocarpine and alcohol. In addition the effect of the laxatives phenolphthalein, castor oil and Epsom salt was investigated. These may act either by increasing peristalsis or the secretion of water into the intestine, or both, according to the laxative employed and the amount. The action of atropine under conditions where a secretion of digestive juices would be expected—after the ingestion of food—was studied and an experiment was carried out to obtain some light on the rôle of muscular work in the excretion of uric acid.

The results of the investigation show that activity of the digestive glands, initiated by the foods mentioned or pilocarpine, is attended by an augmented excretion of uric acid. The laxatives showed no influence on the excretion of uric acid even when agar agar was taken previously for the purpose of increasing the mechanical work of the intestine. Neither did alcohol or muscular exercise. Atropine inhibited the rise which normally follows the ingestion of the food-stuffs taken subsequent to the atropine.

90 (1022)

The mechanism of the action of anti-pneumococcic serum.

By CARROLL G. BULL, M.D.

[*From the Laboratories of the Rockefeller Institute for Medical Research.*]

A year ago it was observed that an intravenous injection of a small amount (0.2 c.c.) of immune serum causes the disappearance, within ten minutes' time, of the bacteria from the blood of a rabbit having a pneumococcic septicæmia. It was decided to investigate the above phenomenon in the hope of ascertaining, if possible, the manner of action of anti-pneumococcic serum.

In the light of our results concerning the behavior of typhoid bacilli in the circulation of normal rabbits, we believed it possible

that whole rabbit blood plus immune serum killed the pneumococci. Therefore rabbit blood was taken in hirudin; varying amounts of immune serum were added to the hirudin blood; definite quantities of bacteria were added and plates made immediately after starting the experiments, and at intervals for twenty-four hours. The colonies were found much reduced in the tubes containing the immune serum and whole blood, but after twenty-four hours all tubes were "saturated" with bacteria. It was believed that the immune serum plus whole blood produced great reduction in the number of bacteria, but could not cause sterilization.

Later it was deemed advisable to follow with the microscope the processes occurring in the tubes. To our surprise, we found that the bacteria were agglutinated in tubes containing serum in a dilution of 1–500; macroscopically the agglutination titre is 1–80. Thus it appeared that the reduction of colonies was due to the clumping.

It was then surmised that the disappearance of the bacteria from the circulating blood of the rabbit following the injection of immune serum might be due to clumping *in vivo* and filtration by the capillary systems of the organs. Our investigation of this point gave the following results:

When a rabbit with pneumococcic septicemia is given 1 c.c. of immune serum intravenously, the cocci are clumped within forty seconds' time and after two minutes they have left the circulation. We have found the clumps in the heart's blood. Next, fragments of the organs—lungs, spleen, liver, kidney, brain, etc.—were crushed and examined, and clumps of pneumococci were found in all. The fate of the clumps was then investigated. By killing the animals at various times after the administration of the serum, it was observed that the polymorphonuclear leucocytes englobed and digested them. The fixed cells play a small part also. Sectioned and crushed tissues gave the same results. Pneumococci from 150 c.c. of bouillon are thus destroyed within two to three hours. The smallest amount of serum that will influence the infection causes the clumping *in vivo*.

Typhoid bacilli, dysentery bacilli, streptococci, staphylococci, and gonococci have been tested for agglutination *in vivo* and all behave in a manner similar to the pneumococci, that is, they

agglutinate in less than one minute's time. Cross-agglutination of the different types of pneumococci was tested and in no case did a heterologous serum cause any clumping. One cubic centimeter of serum per kilo of body weight was given in these cross tests.

The phagocytosis is enhanced by the accumulation of the polymorphonuclear leucocytes in the capillaries of the organs immediately after the injection of the serum. These observations corroborate the findings of Goldscheider and Jakob, that the leucopenia following intravenous injections of protein substances is due to accumulation of the leucocytes in the lungs and other organs, and not to a destruction of the cells. They also prove that the leucocytes are not killed or injured by the intravenous injection of such substances, but are still actively phagocytic.

91 (1023)

Notes on the surgical physiology of the dog.

By **W. HOWARD BARBER** and **JOHN W. DRAPER.**

[*From the Laboratory of Experimental Surgery, N. Y. University.*]

1. HYDRONEPHROSIS AND HYDROURETER.

In a previous communication[1] the possible causal relationship of a paralyzed ureter to dilatations of the ureter and kidney pelvis has been pointed out. Of the experiments performed in 1913, 75 per cent. showed hydronephrosis in some degree. Last fall the same technic was repeated in twelve dogs with the following results:

2 Negative.
6 Hydronephrosis—to some degree.
1 Hydroureter.
3 Dilatation of cephalad ureter.

Therefore fifty per cent. showed hydronephrotic change and eighty-three and one-third per cent. hydronephrotic and hydroureteric changes combined.

It was realized in applying this information to the origination of a physiological uretero-sigmoid union, some traumatization of

[1] Stewart and Barber, Hydronephrosis, Annals of Surgery, Dec., 1914, Barber and Draper, Renal infection, *Jour. Amer. Med. Assoc.*, Jan., 1915.

the transposed ureter and therefore some impairment of ureteric function was absolutely unavoidable. But making allowance for this reduced prostaltic power by the least possible *total* ureteral traumatization and by purposely confining the necessary handling to the negligible caudad third, an effort has been made to balance such impaired power by a physiologic load. To this end twenty dogs have been operated upon by transplanting one ureter in seven and both ureters in thirteen dogs. The results were as follows:

1. Direct uretero-sigmoidal entrance was found more obstructive than the oblique entrance.

2. When ureteral dilatation occurred it appeared first in the cephalad third of the ureter. This was associated in the animals having greater caudad obstruction with dilatation of the second or second and caudad thirds of the ureter and renal pelvis.

3. Each of the seven dogs with singly transplanted ureters showed hydronephrosis in some degree. The ureter in each case had been made to enter the sigmoid directly or obliquely for not over 0.5 cm.

4. Of the thirteen with doubly transplanted ureters, three showed cephalad ureteral dilatation only. These were dogs in which the ureters traversed the sigmoidal wall for 1.5 cm. The thirteenth dog with an intramural ureteral segment of 2 cm. on one side and a direct entrance on the opposing side after seventeen days of life, showed a normal kidney and ureter on the oblique and a pyonephrosis on the direct side.

2. ENTERIC DILATATION.

A. Small Intestine.

Fourteen animals have been incompletely obstructed about the iliocecal region to determine a possible dynamic change in the cephalad end of the small intestine. The conclusions have been these:

1. A fixed diameter of the caudad ileum of approximately 1 cm. (incomplete obstruction) is followed in 5.8 days by a dilatation of a duodenum of mean volume of 12.2 c.c. to a mean volume of 19.2 c.c.

2. A fixed caudad ileac diameter of 0 (complete obstruction) is followed by a contraction of a mean duodenum of 14 c.c. to a mean of 6.25 c.c. in five days. A similar result was noted after acute gangrenous typhlitis and incomplete obstruction of the cephalad colon.

B. Colon.

Six experiments have been performed on the colon. Incomplete obstruction of the extreme caudad colon for a mean of 10.75 days was followed by a dilatation of a cecum of a mean volume of 18 c.c. to a cecum of 29.5 c.c.

92 (1024)

Nephelometric study of the proteins of cerebro spinal fluids.

I. RELATION OF EUGLOBULIN, TOTAL-GLOBULIN AND TOTAL-PROTEIN TO WASSERMANN REACTION.

By **J. A. F. PFEIFFER, PHILIP ADOLPH KOBER** and **CYRUS W. FIELD.**

[*From the Government Hospital for the Insane, Wash., D. C., the Harriman Research Laboratory, Roosevelt Hospital, N. Y. City and the Pathological Laboratory, Bellevue Hospital, N. Y. City.*]

INTRODUCTION.

In syphilitic diseases of the nervous system the composition of the cerebrospinal fluid has become of increasing importance. On the exact chemical picture of the fluid, especially from a quantitative standpoint nothing has been done. It is true, the proteins and to some extent the phosphorus have been roughly estimated and in some cases correlated to the Wassermann reaction.

For this deficiency of quantitative data the reason is found in the lack of material; the present chemical methods used heretofore having been too crude for the low concentration of substances in the very small amounts of fluid.

Since the development of nephelometry the quantitative

estimation of many of the substances occurring in minute amounts in the body is a comparatively simple matter.

In the hope of getting useful information, we have studied quantitatively the proteins of cerebrospinal fluids with nephelometric methods, and have correlated our findings with the Wassermann reaction and other tests.

TECHNIC.

The spinal fluid was accurately measured in a small graduated cylinder or centrifuge tube, and an equal volume of .2 per cent. tricresol added as a preservative.[1] This preserved the fluids for a week or longer.

For the *total-protein* estimation 2 c.c. of diluted fluid (corresponding to 1 c.c. of original) were diluted with 8 c.c. of distilled water, and then precipitated with 20 c.c. of 3 per cent. sulphosalicylic acid. If the amounts of fluid were small, one half or one third these amounts were used.

This suspension was then matched in the nephelometer[2] with a standard made by adding 20 c.c. of 3 per cent. sulphosalicylic acid to 10 c.c. of a .01 per cent. solution of casein. The readings gave at once, upon calculation, the milligrams of total protein in 1 c.c. of spinal fluid. If the standard was much stronger than the "unknowns" a weaker casein solution was used, *e. g.*, .005 per cent., .0025 per cent., .00125 per cent.

For the *total globulin* estimation 2 c.c. of diluted fluid (1 c.c. of original) were diluted with 3 c.c. .1*N* acetic acid and 5 c.c. of saturated ammonium sulphate solution. This was also matched to a casein standard as in the total-protein estimation. Theoretically the standard should be of the same substance as the one to be determined, yet here it seemed best to refer all the estimations to an arbitrary standard for the sake of uniformity, speed and convenience, as pure samples of these proteins are very difficult to obtain.

The *euglobulin content* in spinal fluid has been determined heretofore by one third saturation of ammonium sulphate, but

[1] S. S. Graves and P. A. Kober, *Journal of Amer. Chem. Soc.*, XXXVI, 751 (1914).

[2] Kober, *Journal of Biolog. Chem.*, 13, 485 (1913); *Journal of Amer. Chem. Soc.*, 35, 290 (1913); ibid., 1585.

recent results by Harriet Chick and others have shown that this is not a sharp method for separating euglobulin from the other globulins. Its most characteristic property is its insolubility at its isolectric point, but owing to its low concentration (.001 to .020 per cent.) in spinal fluids the estimation in this way has never been attempted heretofore.

From the diluted spinal fluid the euglobulin is precipitated by adding a trace of acid to help free it from its alkaline salt, and diluting. The diluting not only tends to hydrolyze any unneutralized salt of euglobulin but decreases any solvent action due to electrolytes.

To 2 c.c. of diluted spinal fluid were added 0.50 c.c. .01*N* acetic acid and 10.00 c.c. of distilled water, and after waiting a few minutes the suspension was matched with a known casein solution (see total-protein estimation).

It may have occasionally happened that the amount of .01*N* acetic acid was either too much or too little, in which case a slight error resulted, but all the figures given here were obtained in that way, using 0.50 c.c. .01*N* acetic acid.

The Wassermann reactions were performed as described by Field in the *Archives for Internal Medicine*, 13, 790 (1914) and the *Jour. Amer. Med. Assoc.*, 62, 1620 (1914).

The chemical and Wassermann tests were made independently, without duplicates, in separate institutions, and the figures were not compared until the end of the series.

The results with *total protein* estimations show, assuming that figures above .050 per cent. indicated pathological increase, that 34 cases out of 51 agreed with positive Wassermann reactions, while 48 out of 54 agreed with negative Wassermann reactions.

Similarly, the figures of the *total globulin* estimation showed, assuming .020 per cent. or less as normal, that 24 cases out of 31 agreed with positive Wassermann reaction, while 44 out of 54 cases agreed with negative Wassermann reactions.

The *euglobulin* content seemed to show remarkably close agreement to the Wassermann test: those above .004 per cent. agreed with positive Wassermann test in 14 out of 16 cases, and those below .004 per cent. agreed with a negative Wassermann reaction in 33 out of 35 cases. Of these 4 discrepancies we have good reasons to doubt the figures obtained in at least 2 of them.

RESULTS.

TABLE I.

No.	Hospital No.	Total Protein, Per Cent.	Total Globulin, Per Cent.	Euglobulin, Per Cent.	Wassermann Reaction.		Diagnosis.
					Fluid.	Blood.	
74	2662	.087		.011	+		Cerebrospinal syphilis
75	2661	.013		.0	−		Questionable.
76	2660	.027		.0	−		Thrombosis.
77	2754	.069		.011	+		General paresis.
78	2752	.072		.014	+	+	" "
79	2746	.051		0	−	−	G. P.?
80	2691	.029		.002	−	−	G. P.
81	2677	.124		0	−	−	G. P.
82	2930	.041		.005	+	+	Cerebrospinal syphilis.
83	2922	.036		0	−		" "?
84	2920	.044		.002	−		G. P.?
85	2919	.043		0	−		Comitose.
86	2912	.040		0	−		G. P.
87	2909	.203	.053	.010	+		G. P. alcoholic.
88	2850	.054		.008	+	+	G. P.
89	2829	.042		.001	−		G. P.
90	2800	.030		0	−	+	G. P.
91	2792	.026		0	−	−	G. P.
92	3461	.016	.008	0	−	−	G. P.?
93	3463	.033	.008	0	−	−	G. P.?
94	3510	.012	.006	0	−	−	Rachitic bronchitis.
95	3610	.029	.006	0	−	−	Uræmia.
96	3628	.023	.007	0	−	−	Hysteria.
97	3584			.006	−	−	G. P.?
98	3586	.024	.008	0	−	−	G. P.?
99	3588			0	−	−	G. P.?
100	3590	.023	.010	0	−	−	G. P.?
101	3595			.008	−	+	G. P.?
102	3939	.049	.002	(.004)	−	−	G. P.
103	3942	.048	.015	.003	+	+	G. P.
104	3944	.044	.003	.001	−	−	G. P.?
105	3945	.097	(.020)	.020	+	+	G. P.
106	3947	.101	.032	.020	+	+	G. P.
107	3950	.044	.001	0	−	−	G. P.?
108	3952			.001	−	−	G. P.?
109	3953	.040	.008	.002	−	−	G. P.?
110	4129	.091	.024	.011	+	+	G. P.
111	4120	.022	.009	0	−	−	Gas poisoning.
112	4113	.047	.010	.005	+	+	Cerebrospinal syphilis.
113	4110	.105	.032	.029	+	+	G. P.
114	4108	.014		0	+(5)	−	Syphilis.
115	4063	.107	.032	.025	+	+	G. P.
116	4065	.033	.011	0	−	−	G. P.?
117	4071	.033	.012	0	−	−	G. P.?
118	4083	.026	.009	0	−	−	G. P.?
119	4087	.027	.010	0	−	−	G. P.?
120	3985	.020	.012	0	−	−	G. P.?
121	3975	.058	.022	.010	+	+	G. P.?
122	3968	.063	.019	.003	−	−	G. P.?
123	3961	.051	.021	.016	+	+	G. P.

SUMMARY.

In this series an increase in the euglobulin fraction appears to run parallel with a positive Wassermann reaction and vice versa. But what the exact normal limits of the euglobulin content are cannot be determined with certainty from this small series of cases. Not until results from a much larger number of cases are obtained can any positive statement be made. We can only claim that the findings are most suggestive. We are continuing the work along these lines on blood as well as on spinal fluids.

93 (1025)

The blastophthoric effect of chronic lead poisoning: Breeding experiments. Preliminary report.

By CARL VERNON WELLER, A.B., M.D. (*by invitation.*)

[*From the Department of Pathology, University of Michigan.*]

There have been frequent clinical observations of the apparent deleterious effect upon the germ plasm exerted by chronic lead poisoning. A majority of these cases have been found in female lead workers and in these it might be supposed that abortions, stillbirths and early deaths of infants were due as much to the toxic effect of lead during intra-uterine development as to an actual injury to the germ plasm. In the smaller number of instances in which the male parent alone was poisoned, the resulting sterility without impotency, the stillbirths and the early deaths of offspring are difficult to explain unless they are due to blastophthoria. The work of Stockard and of Cole and Davis has shown that alcohol has a similar effect. In a recent report which appeared as the present series of experiments was being concluded Cole and Bachhuber have demonstrated that the offspring of male rabbits poisoned by lead as well as of male fowls similarly poisoned are of distinctly lower vitality than the offspring of normal males.

In attempting to determine experimentally whether blastophthoria occurs in chronic lead poisoning, guinea pigs were given repeated weighed doses of commercial white lead in capsules by

mouth. These guinea-pigs were mated, lead females with normal males and lead males with normal females. In order to check the results as efficiently as possible control matings were made of normal males with normal females under the same feeding and housing conditions as the lead poisoned pigs, and for the same reason the normal females were bred alternately to lead males and to normal males. The dosage of lead was controlled by frequent weighings in order that the general nutrition should not be seriously impaired.

A total of 93 matings yielded 170 offspring. Of these, 32 matings of normal male with normal female produced 58 offspring with an average birthweight of 81.5 gms. From 34 matings of lead male with normal female 65 young were produced with an average birthweight of but 66.3 gm. From 27 matings of normal male and lead female, 47 young were produced with an average birthweight of 69.3 gm. Nine offspring of lead males died in the first week against two offspring of normal males dying in that time. Eight young of lead females were stillborn against three stillborn from normal females bred to normal males.

From the entire series of matings the following conclusions seem to be justified:

1. In chronic lead poisoning in guinea pigs there is a definite blastophthoric effect which can best be demonstrated upon the male germ plasm. This effect manifests itself in some instances by sterility without loss of sexual activity, by a reduction of 20 per cent. in the average birthweight, by an increased number of deaths in the first week of life and by a retardation in development such that these pigs remain permanently underweight.

2. From the apparent recovery of the germ plasm some time after stopping the administration of lead it seems that the deleterious effect must be suffered especially by that portion of the germ plasm which is undergoing maturation and not by that which is stored in the primary germinal epithelium. However, final judgment upon this point must be withheld.

94 (1026)

Experimental calcification.

By OSKAR KLOTZ and MAY E. BOTHWELL.

[*From the Pathological Laboratories, University of Pittsburgh, Pittsburgh, Pa.*]

In 1905[1]–6[2] one of us was interested in the process of pathological calcification and indicated that in the human the condition was directly related to an antecedent fatty change in the tissues. From the studies then made it was demonstrated that the main factor leading to calcification of diseased organs was the accumulation of fatty materials in necrotic areas. The fat in these areas was liberated by the death of cells or was attracted to the areas of necrosis by the products of disintegration. The latter has been further demonstrated in the accumulation of fat by hyaline and amyloid substances.

Further proof of the relationship of fatty materials to the process of calcification is offered in a series of experiments where fats have been inoculated intravenously into rabbits. Two rabbits have been inoculated with pure olive oil and three with a mixture of cholesterin and olive oil (1–15) by the ear vein. Doses of 0.5 to 1 c.c. were given over a period of from one to eight weeks. The animals withstood the inoculations very well and showed no loss in weight. Temporary respiratory difficulty was sometimes observed for the first hour. The cholesterin mixture was usually warmed before giving.

The best results were obtained with the cholesterin-olive oil mixture after a period of four weeks. The major quantity of the oily injection was filtered out by the lung capillaries and only relatively small amounts reached the distant organs in its original condition. Reactions were recognized in the lung tissue at the end of two weeks when active proliferation of the endothelial lining of the capillaries frequently occluded their lumina or distorted the channels of the arterioles. The proliferating endothelium phagocyted the oil globules and frequently split the

[1] *Journal Exper. Med.*, 1905, VII, p. 633.

[2] *Journal Exper. Med.*, 1906, VIII, p. 322.

larger masses into small fragments which then were scattered through the protoplasm of these cells. The intracellular position of the fat could be observed during all stages of the experiment. In other instances, the phagocyted fat was removed from the blood channels and passed to the lymphatics. Such fat then appeared to lie free and not within cells. In the arterioles the fat appeared both in the proliferating endothelial cells as well as in deeper portions of the intima and media. In the latter structure it was commonly observed as an extracellular deposit. It was not uncommonly seen that the endothelial cells contained both fatty masses and cholesterin crystals. These crystals lay in clefts quite apart from the oil globules.

By staining with sudan all the oil masses were equally colored. Sections stained with Nile blue sulphate showed the presence of neutral fats, fatty acids, and intermediate mixtures of these. With the polarizing microscope some anisotropic globules could be seen, while free cholesterin plates were also demonstrated. The majority of the fatty acid globules were intracellular. These were usually smaller than the globules of neutral fat. The fatty acid racidal was also demonstrated by the Fischler method.

Associated with the intra- and extra-cellular fatty acid globules, was found the deposition of calcium salts. The calcium became precipitated in the borders of these fatty acids and gradually irregular calcium precipitates encroached upon the center of the acid globule. This deposit took place in the protoplasm of the large phagocytic cells as well as in the fatty deposits which were lying free in the tissue or in the lymph channels. At the end of eight weeks we found the lung substance filled with these minute calcareous masses lying in areas of cell proliferation looking not unlike small tubercles. The calcareous process was also recognized in the walls of the blood vessels. In the latter, the process occurred in the deep intima and media where fatty deposits were also demonstrated. These calcium salts were recognized by staining with hematoxylin and their phosphatic radicals with silver nitrate. They could be removed by treating the tissue with hydrochloric acid.

By the method here employed one is able to demonstrate the intimate association between the abnormal presence of fats and

the process of calcification. It is furthermore shown that the endothelial cells of the capillaries of the lungs have the property of splitting fats and liberating the fatty acid radical. By microchemical means the stages in the process may readily be followed.

As the fat within the endothelial cells has been phagocyted and lies in vacuoles in the protoplasm where it is acted upon by lipolytic secretions of the cell, it differs but little, in relation to cell activity, from fatty deposits which are extracellular and are acted upon by lipases present in the serum. In other words, the phagocyted fat of endothelial cells has an entirely different bearing to the cell from the accumulation of fats in fatty degeneration.

Our present findings are in perfect accord with the views we have formerly expressed upon the process of pathological calcification.

95 (1027)

Tumor-like growths in rat stomach following irritation.

By **F. D. BULLOCK** and **G. L. ROHDENBURG.**

[*From Columbia University, George Crocker Special Research Fund, F. C. Wood, Director.*]

Fibiger's announcement of the production of carcinoma in the rat stomach through the agency of nematodes has not as yet been controverted. We wish briefly to record the fact that somewhat similar pictures can be produced by other means of irritation. By suspending in the stomach cavity woolen balls saturated with chemical irritants or by injecting the chemical irritants into the wall itself, polypoid growths of stratified squamous epithelium can be produced. By using celluloid balls with spinous processes these polypoid growths can be made to reach considerable dimensions. When these irritants are applied to the glandular portions of the organ, marked localized thickenings of the mucosa are produced. The chemical irritants cause a marked downgrowth of stratified epithelium resembling the cancroid type described by Fibiger, while the mechanically induced proliferations are characterized by a marked overgrowth of the cornified layers and relatively slight downgrowth. In the glandular por-

tions of the organ the proliferation under chemical irritation assumes the character of a cystadenoma which involves the stomach wall to a considerable depth.

96 (1028)

The inhibition of peristalsis by the oil of chenopodium.

By WILLIAM SALANT and C. W. MITCHELL.

[*From the Pharmacological Laboratory, Bureau of Chemistry, U. S. Department of Agriculture, Washington, D. C.*]

Most of the observations were made on isolated segments of intestine taken from different animals and placed in Locke's solution through which a constant stream of oxygen was allowed to pass. Oil of chenopodium added to Locke's solution produced a marked decrease of contractility. An emulsion of 1 : 10,000 oil of chenopodium decreased the force and frequency of the contractions soon after the gut was exposed to the oil. When subjected to the influence of oil of chenopodium for a short time, 10 to 15 minutes, recovery, though incomplete, took place if at the end of this time it was returned to Locke's solution alone. When the tissue remained longer in contact with the oil, recovery was slight if Locke's solution was substituted for an emulsion containing oil of chenopodium. The depressing effect of chenopodium was found to vary in different portions of the gut, being much more marked in case of the colon than in segments taken from the small intestine.

The intravenous injection of chenopodium given in the form of an emulsion with neutral olive oil or cocoanut oil and acacia inhibited peristalsis. One tenth to 0.125 c.c. of the oil of chenopodium was followed by decreased frequency of peristaltic action and in some experiments the administration of 0.125 to 0.2 c.c. per kilo completely abolished the movements of the cecum for a considerable period of time.

97 (1029)

Further observations on the toxicity of the oil of chenopodium.

By WILLIAM SALANT and ROBERT BENGIS.

[*From the Pharmacological Laboratory, Bureau of Chemistry, U. S. Department of Agriculture, Washington, D. C.*]

As pointed out in a previous communication from this laboratory, the vegetable oils may decrease the toxicity of the oil of chenopodium. Observations made since these results were published, have amply corroborated our previous findings. Four tenths to 0.6 c.c. per kilo of the oil of chenopodium given by mouth to rabbits was fatal in 22 per cent. to 25 per cent. of the experiments while the mortality when this amount was given in acacia reached 78 per cent. Observations were also made on the effect of chenopodium on the action of the kidney under different conditions of diet. Albumin and casts were found in the urine after the administration of 0.4 to 0.6 c.c. oil of chenopodium per kilo with 15 c.c. cocoanut oil to rabbits receiving an oats diet. A small amount of albuminuria and casts were also found, however, after feeding the same amounts of the vegetable oils. This usually lasted 24 to 48 hours, while albuminuria and casts after oil of chenopodium persisted much longer. When oil of chenopodium was given in acacia similar results were obtained indicating that the glycerides do not protect the kidney against the irritating effect of oil of chenopodium. On the other hand, in experiments on rabbits which received carrots the results indicated a very marked protective action. Four tenths to 0.6 c.c. oil of chenopodium per kilo fed to rabbits on such a diet usually failed to indicate the presence of renal irritation. Albumin and casts seldom appeared in the urine especially when a sufficient amount of carrots was consumed. The functional efficiency as tested by the elimination of phenolsulphophthalein did not show any evidence of impairment in rabbits and dogs. The permeability of the kidney is distinctly interfered with, however, in poisoning with oil of chenopodium. We found that fat soluble dyes may pass into the urine of normal rabbits. But when chenopodium is given at

the same time or several days later, the elimination of these dyes may be partly or entirely inhibited. In some experiments, permanent arrest of the passage of these substances was caused by the administration of chenopodium.

98 (1030)

An index of urea excretion.

By FRANKLIN C. MCLEAN.

[*From the Hospital of the Rockefeller Institute for Medical Research, New York.*]

Ambard and Weill have expressed the relationship between the concentration of urea in the blood and the rate of its excretion by means of a formula known as Ambard's coefficient,[1] the accuracy of which has been confirmed on a number of normal individuals by the author and Selling.[2] We now use the Ambard laws in a new formula, which expresses the ability of the kidney to excrete urea in percentage of the normal efficiency.

$$I \text{ (Index)} = \frac{8.96\, D \sqrt{C}}{Wt \times Ur^2}.$$

I = index of urea excretion (100 = average normal, 80–150 maximum normal variation).
D = grams urea excreted per twenty-four hours.
C = grams urea per liter of urine.
Ur = grams urea per liter blood.
Wt = weight of individual in kilos.

The index measures directly one of the more important functions of the kidney and has yielded valuable data in the study of various conditions associated with impaired elimination. For the calculation a special slide rule has been devised, which enables one to make the necessary calculation without effort in a few seconds.

[1] Ambard, *Compt. rend. Soc. de biol.*, 1910, Dec. 3, p. 506.
[2] McLean and Selling, *Jour. Biol. Chem.*, 1914, XIX, 31.

99 (1031)

The nature and detection of diabetic acidosis.

By DONALD D. VAN SLYKE, EDGAR STILLMAN and GLENN E. CULLEN.

[*From the Hospital of the Rockefeller Institute for Medical Research, New York.*]

Simultaneous determinations by the following three methods were made on diabetics in various stages of acidosis.

1. *The alveolar carbon dioxide, by Fredericia's method.*

2. *The carbon dioxide capacity of the oxalate plasma.* The plasma is shaken with air containing 6 per cent. CO_2, and the CO_2 content of the plasma is then determined. A simple apparatus was devised which permits, in three or four minutes, a determination of the CO_2 content, with an accuracy within one per cent. It consists essentially of a 50 c.c. pipette, provided with three-way stopcocks at the top and bottom, and connected with a mercury bulb. The pipette being full of mercury, 1 c.c. of plasma, washed in with 1 c.c. of water and 0.5 c.c. of $N/1$ acid, is introduced through the upper cock. The mercury is then drawn out from below by lowering the mercury bulb until a Torricellian vacuum is obtained in the pipette. The carbon dioxide escapes from the solution as the result of a few seconds shaking, and the water solution is drawn out of the pipette at the bottom. The mercury is then let in again through the other entrance of the 3-way cock at the bottom, and the volume of the carbon dioxide is read in the upper stem of the pipette, which is calibrated in 0.02 c.c. divisions. Normal serum binds about 75 per cent. of its volume of CO_2. In acidosis we have seen the figure as low as 20 per cent.

3. *The H^+ concentration of the plasma after addition of known amounts of HCl.* The H^+ concentration of the untreated plasma itself is about the same in normal condition and in acidosis. In the latter condition, however, as follows from the reasoning of L. J. Henderson, the ability of the blood to maintain its reaction when treated with acid must be lowered. This is demonstrated by our results. Addition of 1 volume of $N/50$ HCl to normal

plasma, previously freed from CO_2 gas in a vacuum, gives a practically neutral solution ($P_H = 7.0$). Plasma from patients in acidosis has been observed to give a $P_H = 4.8$ under the same conditions. The results by this method run parallel to those by the CO_2 capacity method, and both blood analyses give figures from which the alveolar CO_2 tension can be predicted within about 5 mm.

The above results indicate that while in acidosis the H^+ concentration of the blood is not altered, its *reserve alkalinity* (ability to retain normal reaction despite addition of acid) is decreased, and that the decrease can be measured by any of the above three methods.

100 (1032)

The Abderhalden reaction II.

By **DONALD D. VAN SLYKE, MIRIAM VINOGRAD** and **J. R. LOSEE.**

[*From the Rockefeller Institute and the Lying-In Hospital, New York.*]

The technique described in the PROCEEDINGS for May 20, 1914, has been modified to the following, which permits more accurate determination of small differences in proteolysis as measured by the amino acid nitrogen: 0.1 gram of dried placenta substrate, or an approximate equivalent of wet substrate, prepared according to Abderhalden, is incubated with 2 c.c. of serum. The mixture is then diluted with about 20 c.c. of water, heated to boiling, and Merck's dialyzed ferric hydrate (Rona-Michaelis method) is added, 1 c.c. for serum alone, 2 c.c. for serum and substrate. The excess iron is precipitated by adding 0.5 c.c. of 1 : 1 solution of crystalline $MgSO_4$, and the solution is filtered and washed into a small evaporating dish. The solution is concentrated on the water bath to dryness; the residue is redissolved in a few drops of water, and washed completely into the micro-amino-nitrogen apparatus. Serum alone gives 0.18 to 0.28 c.c. of nitrogen gas, duplicates on the same serum agreeing within 0.01 c.c. or closer. The increase due to placenta may be as high as 0.25 c.c. Normal male sera give results varying over about the same range as pregnant sera, although a somewhat greater proportion of pregnant than of male sera give results near the upper limit of the range.

101 (1033)

The shape of the human red blood corpuscle.

By H. E. JORDAN.

[*From the Department of Anatomy, University of Virginia.*]

In a paper published in 1909[1] I presented evidence in refutation of the new teaching[2] that the normal shape of the mammalian red blood-corpuscle is cup-form. This evidence included data derived from an examination of the capillaries in the omentum of an anesthetized cat, sections of variously fixed tissues, and hanging drop preparations of fresh blood. The latter, sealed and kept at body temperature, were thought to simulate closely actual conditions in the blood vessels of the living animal. The free central corpuscles of such a drop preparation are almost exclusively of the circular biconcave disc form. In view of all the evidence there seemed to be no escape from the conclusion that the biconcave disc-shape is the normal, the cup-shape the derived, form of the mammalian erythroplastid. But since opinion still remains divided on the point as to what is the original and normal shape—that is, whether cup or disc—additional evidence is demanded. Cogent confirmatory data accrue from observations of the corpuscles in the gelatin solution recently devised by Hogan[3] as a substitute for salt solutions for transfusion purposes in clinical cases calling for relief to a fall in blood pressure. The special point of advantage claimed for Hogan's normal-salt-gelatin mixture is that it has the colloidal constitution of blood plasma, and in consequence is not lost from the blood vessels through secretion and osmotic processes as salt solutions are supposed to escape.

The method of procedure in my investigation was to place the Hogan's solution[4] in an incubator at a temperature of 42° C. Hollow ground culture slides, cover slips, a pipette, and a needle were also kept in the same incubator. The excess above the

[1] *Anat. Anz.*, 34: 16.

[2] Weidenreich; Lewis; et al.

[3] *Journ. Amer. Med. Assoc.*, 64: 9, 1915.

[4] I am indebted to Dr. H. T. Marshall for assistance in the preparation of this solution.

normal body temperature was planned to compensate for the cooling incident to the frequent opening of the incubator and the transfer of the preparation for study to the microscope stage. The microscope was used exposed to direct sunlight, and the room temperature was about 73° F. A ring of vaseline was spread around the depression in the slide, which was then filled with the solution by means of the warm pipette. The finger was then pricked with the needle, dipped into the stock solution in the incubator, blood squeezed into the adherent drop, and the resulting mixture touched to the solution on the slide. The mount was quickly covered with a warm cover glass and placed under the microscope for study.

Many of the corpuscles sink at once in masses to the bottom of the concavity in the slide. Those at the periphery almost instantly form long rouleaux. Occasional complicated groups of rouleaux appear. The individual corpuscles seem somewhat more densely packed and more compressed than in drop preparations of fresh unmixed blood. A rapid preliminary examination revealed not a single indubitable cup-form. Careful searching may discover a few cups in most preparations. Some of the peripheral corpuscles crenate within the space of five minutes, and their number augments for about a quarter of an hour.

The main evidence regarding the shape of the erythroplastids is derived from an examination of the more central, freely suspended, and slowly sinking corpuscles. These are clearly circular biconcave discs. They have a gently quivering motion. Seen in profile they appear dumb-bell-shaped. If a freely moving corpuscle is watched for some time it may be seen to turn upward now one side now the opposite side, in either case showing a central depression. Viewed obliquely such a biconcave disc gives the deceptive appearance of a shallow cup. This optical illusion may account for a certain amount of misinterpretation. The vast majority of the corpuscles remain unaltered at room temperature during the period of observation, the space of an hour. The corpuscles gradually all sink to the bottom of the preparation, but remain disc-shaped, many presenting profile views. A disc may be watched slowly changing into the crenated condition. Placing the slide immediately after preparation on ice for a

moment or two does not apparently increase the number of crenated corpuscles nor the number or size of the rouleaux, indicating that these phenomena are not dependent directly upon a lowering of temperature.

The same technic was employed with several salt solutions (Tyrode's,[1] Ringer's and the 0.9 per cent. "normal"), with essentially the same results. These solutions differ from the gelatine mixture in their effects upon the corpuscles apparently only in that they permit crenation to occur more rapidly and more extensively, and in degrees in the order named. The fact that rouleaux form only in the gelatin solution indicates a closer intrinsic similarity to blood plasma than any of the salt solutions possess.

Cup forms appear most abundantly in ordinary preparations with Ringer's solution when the cover glass is supported by a hair. The explanation that immediately suggests itself is that the floating discs become altered into cups through adjustment to the narrow confines between slide and cover glass. In other words, a cup form is conceived of as a circular biconcave disc which has become pushed out on one or the other of its concave surfaces.

If the above-mentioned solutions, used in the manner described, reproduce sufficiently closely the conditions which obtain within the blood vessels of a living animal, the conclusion is inescapable that the normal original adult shape of the red blood corpuscle is that of a circular biconcave disc as was originally taught. The only conceivable other theoretically more favorable condition is that presented in the mesentery of a living animal; but observations cannot be made without the use of an oil immersion lens, and this involves pressure, which is believed to be the chief factor in the production of cup forms through narrowing the confines to which the delicate discs are compelled to adjust themselves.

[1] *Pflüger's Archiv*, vol. 148, p. 273, 1912.

102 (1034)

A note on the desensitization of rabbits.

By ALFRED H. CAULFEILD, M.B.

[*From the Department of Medical Research, University of Toronto.*]

Twenty-four rabbits had received the following initial doses of bovine protein:

1915, January 16. 5.0 c.c. intrapleuraly.
" 19. 0.5 c.c. subcutaneously.
" 21. 4.0 c.c. intrapleuraly.
" 26. 2.5 c.c. intravenously.
" 30. 5.0 c.c. intrapleuraly.

On March 24, 1915, after an interval of 53 days, all received two subcutaneous doses of 0.02 c.c. and 0.1 c.c. (diluted to 0.5 c.c. with saline) without any disturbance being produced, and on the following day, March 25, two more subcutaneous doses of 0.25 c.c. and 1.0 c.c. In no instance was any disturbance produced throughout the four reinjections.

On March 26 2.0 c.c. was tried intravenously. Five rabbits had been injected when an acute death occurred and this was rapidly followed by a second. For the remaining 21 rabbits (as one had met with an accidental death) the dose was halved to 1.0 c.c. intravenously without any definite disturbance.

On March 28 all received 5.0 c.c. intrapleuraly without any definite evidence of anaphylactic shock, although a number seemed slightly depressed for an hour or so.

RESULTS OF REINJECTIONS IN RABBITS 13 DAYS AFTER LAST INITIAL INJECTION.

Date.....	24.3.15		25.3.15		26.3.15	28.3.15
Dose.....	0.02 c.c.	0.1 c.c.	0.25 c.c.	1.0 c.c.	2.0 c.c. & 1.0 c.c.	5.0 c.c.
Manner..	Subcutaneous		Subcutaneous		Intravenous	Intrapleuraly
Results (deaths)	0	0	0	0	2 in 5 for 2.0 c.c. 0 in 21 for 1.0 c.c	0

103 (1035)

A note on the desensitization of guinea-pigs.

By ALFRED H. CAULFEILD, M.B.

[*From the Department of Medical Research, University of Toronto.*]

During the course of certain experiments it so happened that I desired to reinject a comparatively large number of laboratory animals with bovine protein, and because of the danger of anaphylaxis I attempted to desensitize these before giving the large amounts of protein which I subsequently wished to use. It was in fact an endeavor to safely desensitize both rabbits and guinea-pigs so that large amounts of protein could be reinjected subcutaneously, intravenously and intrapleuraly. The results seemed worth recording both because of their practical bearing and because of one or two striking occurrences.

The number of animals which came into consideration were 72 guinea-pigs. On account of the character of the initial or sensitizing doses they should be divided into two groups, namely a set of 30 and a set of 42.

The former received the following initial injections:

1915, January	16.	2.5 c.c.	subcutaneously.
"	21.	1.0 c.c.	"
"	30.	0.5 c.c.	"
February	2.	1.0 c.c.	"

The set of 42 received only one initial dose of 0.5 c.c. on January 22, 1915.

The first reinjection (subcutaneous) was given on March 24, 1915, an interval of 50 days. It is perhaps advisable to explain the practical carrying out of the injections to make Chart I clear. Both sets of guinea-pigs (all of which were numerically tagged) were put in a large cage and the injections were carried out by taking the animal most convenient, without regard to its number, and transferring immediately after injection to a different cage. The dose first tried was 0.02 c.c. protein diluted to 0.5 c.c. with saline, but before the seventh animal was injected two guinea-pigs were showing toxic symptoms and died immediately. As on

account had been paid to the order in which the animals had been treated it was only possible to ascertain the numbers of the six so treated. From the time necessary, however, for the injections the animals must have died from within one to ten minutes after they had received their injection. Following this the dose was halved (*i. e.*, 0.01 c.c. diluted to 0.5 c.c.) for the remaining 66 animals without a casualty or any signs sufficiently definite that anaphylactic intoxication could with certainty be diagnosed. It so happened that the six animals receiving the higher dose of 0.02 c.c. were all from the set of 42.

The second injection (subcutaneous) was given shortly after completing the first and 0.1 c.c. protein (diluted to 0.5 c.c. with saline) was tried. As before two acute deaths occurred in the six so inoculated. Again the dose was halved, as in the preceding injections, without any fatality for the now remaining 64 animals. This time it so happened that five of the six guinea-pigs, which had received the larger dose, belonged to the set of 30, and both deaths occurred amongst the five, so that there was no evidence that the character of the initial sensitizing dose had had any bearing on the results.

In all four cases death was acute and rapid; the post mortem showed the typical emphysematous condition of the lungs.

The third (subcutaneous) desensitizing dose of 0.125 c.c. protein (diluted to 0.5 c.c. with saline) was given at 11 A.M., and the fourth (subcutaneous) of 0.5 c.c. protein at 4.30 P.M. of the following day, March 25, without any immediate ill effects. The following morning, however, one animal in the set of 42 was found dead. The post mortem showed a most marked condition of general anasarca. On cutting the skin the subcutaneous tissues were very swollen and fluid rapidly oozed from the cut surface, the serous cavities contained a very appreciable amount of free fluid, the lungs were very edematous and the tubes greatly distended with clear fluid.

Following the two injections of the 25th of March, large doses were given on subsequent days without any evidence of toxic symptoms.

Besides the two sets of guinea pigs above, there was also a small set of six which had received an initial dose of 0.5 c.c. goat

serum on January 22, 1915. Reinjection was made on March 24 of 0.01 c.c. and 0.1 c.c. (diluted to 0.5 c.c. with saline) without any ill results. Further injections of larger amounts gave negative results.

These results on guinea-pigs might be gathered together as follows:

1. While the first desensitizing dose was sufficiently strong to cause acute death in two out of the six guinea-pigs, one half the dose failed to cause any marked or certain evidences of anaphylactic poisoning in the remaining 66 animals.

2. While the strength of the second desensitizing dose was sufficiently strong to cause acute death in two out of six guinea-pigs, one half the dose again failed to cause marked or certain evidences of an anaphylactic poisoning in the remaining 64 animals.

3. Two subcutaneous desensitizing doses were given on two successive days and this proved successful in producing a fully refractive state in those that survived.

4. On the night following the fourth dose, which was 0.5 c.c. protein, one pig died and the post mortem showed a marked condition of general anasarca.

5. All injections were made subcutaneously and into approximately the same area.

6. Out of 72 guinea-pigs, previously injected with bovine protein a total of 5 died during the course of desensitization, four in acute anaphylactic shock and one later with general anasarca.

7. Six guinea-pigs showed no little evidence that they were sensitive to goat serum.

CHART 1.

ILLUSTRATING FIRST AND SECOND DESENSITIZING DOSES ON GUINEA-PIGS, 50 DAYS AFTER LAST INITIAL INJECTION.

Time and Date.	First Reinjection Subcutaneously 10:30 a. m., March 24.	Anaphylactic Death in	Second Reinjection Subcutaneously 11:45 a. m., March 24.	Anaphylactic Death in
Set of 30 guinea-pigs	Dose .02 c.c. for 0	0	Dose 1 c.c. for 5	2
	Dose .01 c.c. for 30	0	Dose .05 c.c. for 25	0
Set of 42 guinea-pigs	Dose .02 c.c. for 6	2	Dose .1 c.c. for 1	0
	Dose .01 c.c. for 36	0	Dose .05 c.c. for 39	0

ABSTRACTS OF THE COMMUNICATIONS, PACIFIC COAST BRANCH.

104 (1036)

Further studies on the occurrence of para-hydroxyphenyl-ethylamine in mistletoes.

By ZENO OSTENBERG (by invitation).

[*From the Laboratory of Pharmacology, Stanford Medical School.*]

In continuation of the work carried on in this laboratory on the occurrence of *p*-hydroxyphenyl-ethylamine in a southern mistletoe (*Phoradendron flavescens* Nutt.), it was decided to examine all the species of mistletoe available, and isolate and identify the amines present.

The examination of a commercial fluid extract of European mistletoe (*Viscum album*)[1] showed that a considerable quantity of a mixture of amines was present. From 946 c.c. of the fluid extract there was isolated .660 gram of mixed oxalates of the amines. This yielded .240 gm. of pure *p*-hydroxyphenyl-ethylamine oxalate, m.p. 203°–204° (corr.). The picrate melted at 206° as did that of the picrate of synthetic *p*-hydroxyphenyl-ethylamine. The di-benzoyl derivatives of both the natural and synthetic amine melted at 174° when melted either separately or mixed, provided they were crystallized from hot propyl alcohol (Kahlbaum's), but at 171.5° when crystallized from 50 per cent. propyl or ethyl alcohol. All melting points were made with Anschütz short scale thermometers (tested and found accurate to .2°) in a Roth melting point apparatus, and therefore need no correction and would naturally be somewhat higher than uncorrected readings, but this does not account for the great difference between these melting points and those reported by others. When more material becomes available the reasons for these differences will be carefully investigated.

A platinichloride, isolated from the hydrochlorides of the steam volatile portion of the amines, was heated to 270° when it decomposed without melting. The amount obtained was too small to examine further.

[1] Put up by John Wyeth and Brother, Philadelphia.

For extracting the amines from a sodium carbonate solution free from alcohol, a mixture of 1 part amyl alcohol with 3 parts ether was used, as it is a better solvent than ether alone and does not emulsify like amyl alcohol alone. The amines were recovered by extracting the ether-amyl alcohol mixture with dilute H_2SO_4.

From the fresh plants of *Phoradendron flavescens*, var. *macrophylla* and *Phoradendron californicum* (obtained through the courtesy of Prof. J. J. Thornber, University of Arizona) no amines, precipitable by oxalic acid from ether solution, were obtained. However, they will be examined further.

105 (1037)

On the mechanism of the anaphylactic reaction in smooth muscle. (Preliminary communication.)

By WILLIAM H. MOORE (by invitation).

[*From the Department of Bacteriology and Immunity, Leland Stanford Jr. University.*]

If the uterus of a sensitized guinea-pig is rendered bloodless by transfusing it with Locke's solution, the sensitiveness of the uterine muscle to the foreign proteid is increased.

If the muscle is further freed from tissue lymph and from other diffusible tissue elements by repeated centrifugation in Locke's solution, the sensitiveness is greatly decreased.

If the serum and diffusible tissue elements thus removed are replaced in the muscle by repeatedly centrifuging the muscle in dilute normal guinea-pig serum, the sensitiveness is restored quantitatively.

This would seem to indicate that the reaction of the anaphylactic uterine muscle is dependent upon two factors: (*a*) a factor induced in the fixed cells by the process of sensitization, and (*b*) some normal serum component. It would also indicate the presence of a third element, (*c*) an antitoxic or anti-anaphylactic serum component.

106 (1038)

Comparative physiology of immune and anaphylactic smooth muscle. (Preliminary communication.)

By WILLIAM H. MOORE (by invitation).

[*From the Department of Bacteriology and Immunity, Leland Stanford Jr. University.*]

The typical anaphylactic reaction in smooth muscle (guinea-pig uterus) is a rapid marked contraction, with little or no tendency toward recovery. The muscle usually remains fully contracted at the end of an ordinary experiment (30 to 60 minutes).

The typical reaction in an immune muscle is a similar contraction, followed by a fairly rapid recovery. Relaxation usually begins in from 2 to 3 minutes. The muscle may be fully relaxed by the end of 15 minutes.

If an immune muscle is rendered bloodless by transfusing it with Locke's solution, its reaction to the foreign proteid is increased. The muscle also loses its power of recovery (relaxation) after the contraction. The transfused immune muscle, therefore, reacts in the same way as a transfused anaphylactic muscle.

From this it would appear that the fixed cellular elements are identical in the two muscles, and that the differences in their reaction are due to differences in the circulating substances they contain.

107 (1039)

Relation of dosage to reaction in anaphylactic shock. (Preliminary communication.)

By MARCUS C. TERRY and E. R. ANDREWS (by invitation.)

[*From the Department of Bacteriology and Immunity, Leland Stanford Jr. University.*]

In support of the anaphylatoxic theory of anaphylaxis it has been pointed out that to produce a fatal dose of anaphylatoxin *in vitro* certain quantitative relations must be maintained between the foreign and the anaphylactic serum. An excess of the foreign protein results in the production of a non-fatal dose of the toxin.

That a similar quantitative relation can be demonstrated in anaphylactic animals tested directly with the foreign protein is shown in the following table: Here an excess of the foreign protein above a certain definite dose per body weight results in a decrease in the toxic effects (percentage of deaths).

The guinea-pigs here reported were sensitized by subcutaneous injections with 0.01 c.c. pooled human serum. They were tested 14 days later by intravenous (jugular) injections with pooled human serum. Test dose recorded as c.c. per 200 grams of body weight.

Test Dose.	Animals Tested.	Died.		Per Cent. of Deaths.
		3 to 8 Min.	1 to 3 Hrs.	
Under 0.20 c.c.	8	0	1	*12.5*
0.20–0.31 c.c.	23	12	2	*61*
0.34–0.37 c.c.	5	0	1	*20*
0.40–0.45 c.c.	7	0	1	*14*

108 (1040)

The question of tonus in skeletal muscle.

By THEO. C. BURNETT.

[*From the Rudolph Spreckel's Physiological Laboratory of the University of California.*]

The idea that the tonus of skeletal muscle is dependent upon the sympathetic system, as asserted by De Boer,[1] is an attractive one, as it brings the tonus of striped muscle into the same category with vaso-constriction and vaso-dilation; but De Boer having been criticized by Beritoff,[2] it was determined to work out the problem independently, in order to arrive at a definite conclusion if possible. The work has been done on frogs at intervals during the winter, but it was not intended to publish until the results of experiments on mammals had also been ascertained, if at all. The appearance of an article by Yas Kuno,[3] however, in the current number of the *Journal of Physiology*, has determined me to publish my results on frogs, as they seem to be confirmatory of his findings.

[1] DeBoer, S., *Folia Neuro-biologica*, Vol. 7, 1913, p. 378.

[2] Beritoff, J. S., *Folia Neuro-biologica*, Vol. 8, 1914, p. 421.

[3] Kuno, Yas, *Jour. Physiol.*, Vol. 49, 1915, p. 139.

The method employed was essentially that of De Boer, with the exception that the gastrocnemius to be observed was simply severed from its insertion by cutting through the tendo achilles, and then freeing it as far as possible from the underlying muscles by breaking through the intermuscular septum with a probe. By this means the skin remained intact; a desideratum, as it has been claimed that removal of the skin results in loss of tone. The tendon was attached by a thread to a writing lever, and the leg firmly fixed at the knee joint by a muscle clamp. Briefly, the results obtained were as follows:

When the brain of a frog is pithed, there is a progressive loss of tone in the muscle, due to shock, until a certain maximum lengthening of the muscle is reached in about forty minutes or more. With the recovery from shock, there are usually a number of spontaneous movements, which are registered as contractions of the gastrocnemius, and the muscle after contraction does not lengthen to the same extent as before. One would say it regains a certain amount of tone, but not all by any means. If now the abdomen be opened and the viscera exposed (a necessary proceeding for cutting the rami communicantes), there is again a loss of tone. After fifteen to thirty minutes there is again a maximum lengthening of the muscle, and now cutting the sciatic plexus, or the rami communicantes has no effect, except that the contraction which results from cutting the sciatic is not followed by a "contraction remainder" as was the case after spontaneous contractions with the nervous connections intact.

It seems possible then, that the results obtained by De Boer were due to the effects of the operation rather than to the cutting of the rami communicantes, for it appears from his article that he began his observations at once. It seems clear also that for the present we shall have to hold fast to our old idea that tonus of skeletal muscle is dependent upon the central nervous system, and not on the sympathetic.

SCIENTIFIC PROCEEDINGS.

ABSTRACTS OF COMMUNICATIONS.

Sixty-eighth meeting.

Zoological Laboratory, Columbia University, May 19, 1915.
President Lusk in the chair.

109 (1041)

Studies of urinary and blood nitrogen curves after feeding in the dog.

By **O. H. PERRY PEPPER, M.D.** and **J. HAROLD AUSTIN, M.D.**

[*From the John Herr Musser Department of Research Medicine, University of Pennsylvania.*]

The following studies were designed to show the hourly variations in the normal dog of the total non-protein nitrogen of the blood compared with the output of urine and of the nitrogen in the urine and the effect upon these of various diets and of variations in the water intake.

Eight dogs have been placed on a diet consisting of meat, lard, sugar, sodium chloride, bone ash and water adequate in calories and containing about 0.4 gm. of nitrogen per kilo of body weight. On the sixth day the ration was varied to suit the study; in dogs 2 to 6 being richer in nitrogen, while in dogs 7, 8 and 9 no food was given on the days of the study. The water intake was varied as shown in the table. On the day of the study the animals were catheterized at intervals of two to four hours and at the time of each catheterization 5 c.c. of blood was taken from the jugular vein for estimation of the non-protein nitrogen by Folin's method. The urinary nitrogen was estimated by Kjeldahl. The results are shown in the table.

Conclusions.—The daily variation in the non-protein blood

nitrogen of the normal dog receiving a diet containing 0.4 gm. of nitrogen per kilo is about 9 milligrams, the maximum being reached about two hours after feeding with a return to the original level in about 10 to 14 hours. By feeding excessive quantities of meat the non-protein blood nitrogen may be increased 25 to 40 milligrams in 6 to 8 hours and the original level is usually not reached even at the end of 24 hrs. In one animal (Dog 4) the blood nitrogen did not reach its maximum until 14 hours after feeding; the urinary nitrogen exhibiting a parallel gradual rise; this is probably only to be explained on the basis of slow absorption from the gastrointestinal tract. It is to be observed that this animal received its allotment of water in small doses throughout the day by stomach tube instead of in one large dose with its feeding; this factor may have influenced the rate of absorption.

The curve of the non-protein blood nitrogen in the normal dog after feeding follows closely that of the urinary nitrogen. There is frequently exhibited, however, a further or secondary rise in the blood nitrogen at the time that the diuresis and output of nitrogen in the urine is rapidly decreasing.

In the fasting dog there occurs a gradual fall in blood nitrogen to a minimum of from 12 to 18 milligrams, reached 30 to 48 hours after the last feeding, and followed by a rise in the next few hours to about 25 milligrams at about which level it tends to persist. The urinary nitrogen shows a similar but less pronounced curve.

The amount of urine influences the urinary nitrogen to a much greater extent when the blood and urinary nitrogen values are high than when they are low. Free diuresis induced by the administration of water to the fasting animal has little effect upon the nitrogen curves.

The application of Ambard's formula to these data fails to give a constant figure. Better results are obtained by the use of a somewhat similar but simplified formula, but here also considerable discrepancies occur, and we have been unable to find any formula that will constantly express the relation between blood nitrogen, urinary nitrogen, and urinary amount.

Hour.	Dog 9. Fasting. Water Given Ad Lib. (60 c.c. Taken in 46 Hours).				Hour.	Dog 1. Moderate Nitrogenous Diet; Water with the Feeding. Wt. = 10,870.					Dog 2. High Nitrogenous Diet; Water with Feeding. Wt. = 6,200.					Dog 3. Very High Nitrogenous Diet; Water with Feeding. Wt. = 7,600.				
	Hours Since Feeding.	Urine.[1]		Blood.		Intake.		Urine.		Blood.	Intake.		Urine.		Blood.	Intake.		Urine.		Blood.
		Amt.	N.	N.		N.	Water.	Amt.	N.	N.	N.	Water.	Amt.	N.	N.	N.	Water.	Amt.	N.	N.
10 A. M....	24			20	8:30 A. M.....	0.39	200			23	1	100			19	2.5	200			25
4 P. M....	30	6	0.16	20	10:30 A. M.....			30	.34	28			11	.50	30			11	.52	29
10 P. M....	36	6	0.15	22	12:30 P. M.....			23	.44	25			24	.97	29			35	1.02	39
8:30 A. M.	46	6	0.19	14	2:30 P. M.....			17	.33	22			9	.63	24			30	1.22	42
Noon.....	50	5	0.22	28	4:30 P. M.....			14	.34	25			9	.51	25			20	1.16	41
4 P. M....	54	5	0.25	27	6:30 P. M.....			12	.33	26			8	.37	21			16	.68	29
8 P. M....	58	5	0.19	25	10:30 P. M.....			8	.27	21			3	.13	19			6	.22	34
8:30 A. M.	70	5	0.20	26	8:30 A. M.....			8	.25	24			3	.16	17			9	.47	26

Hour.	Dog 4. Very High Nitrogenous Diet; Water Throughout Day. Wt. = 12,150.					Dog 7. Fasting; Water Once at 8:30 A. M. Wt. = 7,360.					Dog 8. Fasting; No Water.					Dog 5. Very High Nitrogenous Diet; Water with Feeding and Throughout the Day.					Dog 6. Very High Nitrogenous Diet; No Water with Feeding; Water Once at 4:30 P. M.				
	Intake.		Urine.		Blood.	Intake.		Urine.		Blood.	Intake.		Urine.		Blood.	Intake.		Urine.		Blood.	Intake.		Urine.		Blood.
	N.	Water.	Amt.	N.	N.	N.	Water.	Amt.	N.	N.	N.	Water.	Amt.	N.	N.	N.	Water.	Amt.	N.	N.	N.	Water.	Amt.	N.	N.
8:30 A. M.	2.5	40			23	0	200			20	0	0			27	2.5	300			22	2.5	0			20
10:30 A. M.		40	10	.38	31			102	.26	19							40	43	.55	33		0	12	.34	22
12:30 P. M.		40	26	.90	31			33	.17	15			6	.25	25		40	162	1.31	38		0	65	1.39	47
2:30 P. M.		40	35	1.35	37			13	.15	13							40	120	1.47	39		0	72	1.85	53
4:30 P. M.		40	30	1.36	42			7	.13	12			5	.22	18		40	130	1.90	47		300	85	2.23	59
6:30 P. M.		40	28	1.42	44			3.5	.09	16							40	70	1.29	44		0	100	2.20	53
10:30 P. M.		40	31	1.57	50			3.2	.08	21			5	.19	22		40	77	1.55	43		0	52	1.83	55
8:30 A. M.			21	1.16	39			4	.12	24			6	.26	25			46	1.36	43		0	44	1.21	30

Intake = N of mixed diet in gms. per kilo of body weight.
Urine amt. in c.c. per 2 hrs.
N in grams per 2 hrs. (Kjeldahl).
Blood N in milligrams per 100 c.c. of blood (Folin).

[1] The amounts of urine and of nitrogen in the urine are expressed in c.c. and gm. *per 2 hours* for each period.

110 (1042)

Inheritance of temperament.

By **C. B. DAVENPORT.**

[*From the Department of Experimental Evolution, Station for Experimental Evolution, Cold Spring Harbor, Long Island, N. Y.*]

Temperament, which determines mood, is generally recognized as having an hereditary basis. It is obvious, however, that the method of inheritance is not a simple one, but what factors are involved have not hitherto been plain. An examination of 150 matings of two persons the mood of both of whom is known as well as that of their children and that of the children's four grandparents has afforded the means to test various hypotheses of which the following seems to satisfy the conditions very closely. There are two hereditary factors involved in temperament, one of which makes for excitation, the absence of this for self-control. The other factor is one that makes for cheerfulness as opposed to depression; the depression being the more easily possible because of the absence of this factor for cheerfulness or normality. The exciting and the normalizing factors and their absence may be combined in the matings in over 50 ways, but for a given mating the disposition of the offspring follows a definite law and the dispositions occur in certain proportions in a fraternity of brothers and sisters. Dominance in the simplex condition is frequently or usually imperfect so that a clear difference between the disposition of children who receive two doses and only one dose of a factor can be recognized. The exciting factor may occur in the child simultaneously with the factor for normality, in which case the person is constantly or periodically elated and when depressed he is not depressed below the normal. The absence of normality, or depression, may occur without elation, in which case the person is constantly or periodically depressed and when not depressed does not rise above the normal. In still other cases factors for elation and depression may both occur in the individual in which case he may show elation and depression either simultaneously or in succession. The latter gives rise to persons of alternating mood and, in extreme cases, to circular insanity.

III (1043)

The question of fat absorption from the stomach.

By EMIL J. BAUMANN.

[*From the Sheffield Laboratory of Physiological Chemistry, Yale University, New Haven, Connecticut.*]

In 1889, Klemperer and Scheuerlen[1] found that no fat was absorbed from the stomach. They were able to recover 99.5 per cent. of the fat introduced into ligated stomachs of dogs after six hours. Within the last fifteen years, however, a number of investigators have published histological observations, from which they have concluded that gastric fat absorption does occur.

With the hope of obtaining some decisive evidence in relation to this question, two physiological-chemical methods, other than those previously employed, have been applied. Fat was introduced into the ligated stomachs of cats and dogs and a study of blood-fat content made in the one case, and in the second it was attempted to discover whether or not any fat left the lumen of the stomach by the use of fat stained with Sudan III. The animals were kept under anesthesia during the experiments.

In neither case could any fat be shown to leave the stomach, although histological studies of the gastric mucosa of the same animals gave results similar to those reported by Weiss,[2] Lamb,[3] Greene and Skaer[4] and others, showing that histologically demonstrable fat had entered the stomach walls.

Since no fat could be shown to have left the stomach by way of circulating fluids, it is concluded that no absorption occurs. The histological findings are explained by assuming that the fat present in the gastric cells entered by purely physico-chemical processes.

[1] Klemperer and Scheuerlen, *Zeit. f. Klin. Med.*, 1889, **15**, 370.

[2] Weiss, *Pfluger's Arch.*, 1912, **144**, 540.

[3] Lamb, *Jour. Physiol.*, 1910, **40**, xxiii.

[4] Greene and Skaer, *Amer. Jour. Physiol.*, 1912, **29**, xxxvii; *ibid.*, 1913, **32**, 358.

112 (1044)

Changes in blood alkalinity during digestion.

By DONALD D. VAN SLYKE, GLENN E. CULLEN and EDGAR STILLMAN.

[*From the Hospital of the Rockefeller Institute.*]

It has been noticed by former observers that the alveolar carbon dioxide tension usually rises after a meal. Two diametrically opposite explanations have been possible: (1) *Acid* digestion products displace carbon dioxide from the blood, and during the displacement the rate at which carbon dioxide passes from blood to lungs is increased. (2) The blood becomes more *alkaline*, as the result of secretion of gastric hydrochloric acid, or absorption of alkaline digestion products. Consequently the carbon dioxide capacity of the blood is increased, and in equilibrium with it the carbon dioxide tension of the alveolar air rises.

We have determined on each of a number of subjects, in conditions of approximate digestive rest and of digestive activity, the following data: (1) Alveolar carbon dioxide tension; (2) Alkaline reserve of the plasma as indicated by its ability to maintain its alkalinity after addition of acid; (3) Alkaline reserve of the plasma as indicated by the amount of carbon dioxide with which it can combine. The results show that the reserve alkalinity of the plasma *increases* during digestion, the alveolar carbon dioxide increasing simultaneously. The second of the above explanations is therefore correct. The cause of the increase in alkaline reserve is being further studied.

113 (1045)

The effect of previous intravenous injection of pneumococci upon experimental lobar pneumonia produced by the method of intrabronchial insufflation.

By B. S. KLINE and S. J. MELTZER.

[*From the Department of Physiology and Pharmacology of the Rockefeller Institute for Medical Research.*]

We wish to report a result obtained in a series of experiments in which the effect of intravenous injections of pneumococci upon subsequent experimental pneumonia was studied. Forty-nine dogs were used in these experiments. Observations were made upon the extent and morphology of the pneumonic process, the leukocytic reaction, the occurrence of agglutinins and the presence of living organisms in the blood and in the lungs. In one series, the animals were given intravenously each day for five days 0.7 c.c. of a broth culture of pneumococci per kilo of body weight. In another series graduated doses were given, beginning with 0.07 c.c. per kilo of body weight and gradually increased to the fifth and last injection of 0.7 c.c. per kilo. In both series on the sixth day, the dogs were given an intrabronchial injection of pneumococci. With groups of these animals, control dogs were also injected intrabronchially with pneumococci. The animals were killed at intervals from nineteen to forty-nine hours after the intrabronchial injection.

We wish to confine our present report to one significant result namely: the rapid disappearance of the organisms from the pneumonic lungs of the animals previously injected intravenously with pneumococci.

In previous experiments reported from this laboratory living organisms were observed in the lungs of dogs with experimental lobar pneumonia as late as the third day after the beginning of the process. The results of the lung cultures in the present experiments may be seen from the charts.

It is evident from these charts that previous intravenous injections of pneumococci bring about a destructive effect upon

the organisms in the pneumonic lung—the organisms disappear from these lungs much sooner than from the lungs of animals not previously treated.

CHART I.

LUNG CULTURES IN DOGS KILLED IN LESS THAN 36 HOURS.

Controls.		Intravenously Injected.	
Hours.	Colonies.	Hours.	Colonies.
27	Innumerable	28½	0
30½	"	21½	0
29½	"	20	0
33	"	30	0
34	"	34½	0
31½	"	33½	1
20	+	30½	1
23	Very many	21½	1
19	Many	20½	3
23	12 +[1]	27	18
22½	0	29	75
		30	103
		24	Very many
		17 died	+
		20 "	Innumerable
		14 found dead	"

[1] Growth in water of condensation.

CHART II.

LUNG CULTURES IN DOGS KILLED IN LESS THAN 50 HOURS.

Controls.		Intravenously Injected.	
Hours.	Colonies.	Hours.	Colonies.
42	Innumerable	45	0
41	Very many	46	0
49	Many	42	0
42	"	43	0
44½	"	43	0
48	+	41½	0
47	+	46½	0
46	25	46	0
45	3	47	0
48	0	49	0
		47½	13
		46	Very many

114 (1046)

A method of studying the effect of serum upon tissues.

By S. FELDSTEIN, M.D.

[*From the Department of Experimental Therapeutics, Cornell University Medical College.*]

In the investigation of the action of serum ferments on animal tissues chemical methods have been almost exclusively used. Within the last few years the dialysis method developed by Abderhalden has been extensively employed in experimental as well as clinical investigations. While the technique of this method is not as difficult as it is usually assumed to be, at every step of the procedure a not inconsiderable number of errors are likely to creep in. It requires very careful preparation of the substrate, absolutely uniform dialyzing tubes and great care in boiling the dialysate.

The most weighty objection to the dialysis method, however, lies in the fact that it gives only indirect evidence of the enzymatic action of the serum on the tissue. It is due to this fact that recently Bronfenbrenner and others have claimed that a positive Abderhalden test does not show the proteolytic action of the serum on the tissue substrate at all, but that during the incubation of the serum with tissue, the antiferment of the serum becomes adsorbed. The removal of the antiferment exposes the serum proteins to the action of the ferments in the serum and it is their cleavage products which pass into the dialysate and give the positive reaction.

Considerations of this nature led the author more than a year ago to seek for a method of demonstrating the ferment action of serum in the histologic examination of tissues. A priori it was to be expected that early evidence of the chemical changes resulting from ferment action might be shown by alteration in the microscopic appearance and staining reaction of the tissue.

Almost the first specimen examined, that of a boiled guinea-pig placenta exposed to the action of normal and pregnant guinea-pig serum, having fortunately shown a most remarkable difference, the author was encouraged to continue the investigation. Soon

it became evident that the histologic method was so delicate an indicator that unmistakable evidence of the action of normal serum on animal tissue was readily demonstrable. The activity of the serum varies greatly with the species of animal from which the serum is derived. Of those investigated the serum of the cat is apparently one of the most powerful and it is with the normal serum of this animal that the present investigation was chiefly concerned.

The serum was obtained from the jugular vein and immediately centrifuged; in this manner best avoiding the mechanical hemolysis which is likely to occur. At first, in addition to the boiled tissue, we attempted to use formalin and acetone fixed sections but found that these fixatives almost entirely inhibited the action of the serum.

In our more recent work we have used fresh and boiled tissue almost exclusively. The use of fresh tissue theoretically did not promise much, as, on the authority of Abderhalden, it has long been assumed that only in the boiled state do the tissue proteins undergo digestion. Moreover, the work of Longcope and others has shown that serum has a preservative action on tissue. This author, however, calls attention to the fact that in the most superficial layers of the block of tissue immersed in serum, the nuclei do not stain, and it is apparently these changes that we are concerned with in our present investigation. In the use of fresh tissue, the factor of autolysis is involved. But as Launoy has shown with the guinea-pig liver, and as we have been able to confirm, marked histologic evidence of autolysis does not appear within the first 24 hours, if the temperature is kept below 37.5 degrees C. Our sections were incubated from 18–21 hours, and in only a few instances did our controls show marked autolytic changes, when needless to say that particular experiment was rejected.

When boiled tissue was used as substrate, small blocks about 2 cm. in thickness were cut, washed in water, then thrown in physiological salt solution and boiled for fifteen minutes. Frozen sections, 10 microns in thickness, were made of the fresh and boiled organs.

The activity of the serum was determined by a series of dilutions, 1, 1/10, 1/20, etc., in physiological salt solution.

The sections (all of about the same size and thickness) were placed in small test tubes, each containing 1 c.c. of the serum dilution. 1 c.c. of physiological salt solution was the constant control. To each tube was added 1 c.c. of toluol and the whole series incubated at 37.5° C. for 18–21 hours.

The staining was done by means of Delafield's hematoxylen and eosin. All sections of a series were stained in an identical

Delafield's hematoxylen	1 min.
½ per cent. alcohol eosin	10 sec.
85 per cent. alcohol	30 sec.
Oil of origanum	Until clear.
Canada balsam mounting.	

manner. Fresh sections were treated by floating on a slide. drying on blotting paper over the paraffin stove, then staining. Boiled sections were transferred in the moist state to the various solutions, as otherwise they are likely to float off the slide. We have also employed the various fat stains and the Altmann granule stain but have found the simple hematoxylen-eosin adequate.

The most striking changes are found in the nuclei. When exposed to the action of cat serum up to a dilution of 1 : 30, no nuclei are to be seen in the boiled sections. On fresh tissue, contrary to what might have been expected, this action was even more marked, as no nuclei were visible at a dilution of 1 : 120 of the serum. The nuclei either had disappeared entirely or had failed to take the stain. In addition the tissue appeared cloudy, parboiled, and not infrequently cleavage lines ran through the whole specimen. At times, as in the guinea-pig placenta to be shown on the screen, the organ assumed a reticular structure, as in specimens treated by the Spalteholz or Mall's digestion method. At other times, the whole specimen appeared homogeneous, the tissue becoming unrecognizable. Fibrous tissue as the trabeculæ of the spleen and adventitia of vessels stand out distinctly, but the nuclei seem to have disappeared. The appearances were very similar to those observed in autolysis of organs.

When we had established that the titre of activity of cat serum remains constant, *i. e.*, no nuclei in the boiled sections on exposure to a dilution of 1 : 30 or 1 : 40 we injected a cat whose serum was previously tested, with 1 gm. of fresh cat liver freed from blood,

intraperitoneally three times, and tested its serum against cat liver. The action of the serum after the series of injections had increased so that the specimens exposed to a dilution of 1 : 60 resembled histologically the ones previously exposed to 1 : 30, etc. The action on the spleen was not nearly as marked.

The serum of a rabbit, injected with Beebe's nucleoproteids derived from dog thyroid, at a dilution of 1 : 5 had a much more striking action on the fresh dog thyroid than on the dog spleen.

As to the exact interpretation of these changes: They cannot be attributed to bacterial action as toluol was always added in abundant amounts and we have found that not infrequently bacteria failed to grow on culture media when they were kept in the same incubator owing to the evaporation of the toluol. Moreover, in a series examined at intervals of ten minutes, we have found that at the end of an hour, the changes in the histologic appearance of the sections were quite marked; a period of time too short for bacterial action to have taken place. We have also been able to show that while inactivation at 55° C. for one hour failed to destroy this activity of the serum, exposure to 65° C. for one half hour led to complete loss of activity.

From the appearance of the specimens, it is my belief that a number of ferments might be concerned in the production of these striking changes, not only proteases but also peptases and perhaps esterases and nucleases. Sodium fluoride in 0.3 per cent. solution, which is a specific inhibitor of esterase action seemed to weaken the activity of the serum. With normal serum extracted by chloroform according to the method advised recently by Jobling, we have not obtained uniform results. When the serum after filtration remained turbid, as was often the case, no action on the tissue was demonstrable. This activity of the serum is apparently not identical with that of trypsin. With the latter, there is marked fragmentation of the sections at a time when nuclei are still visible. While the present investigation was in progress, there appeared a brief preliminary communication in the *Muenchener medicinische Wochenschrift*, No. 37, 1914, by H. Rollett, describing a method by which bits of boiled placenta were exposed to serum, then examined histologically. Very meager details are given.

Dr. W. L. Rost has assisted me in most of the experiments of the present investigation.

115 (1047)

The effect of sensitization on pneumococcus lesions of the lobar type in rabbits.

By MARY B. KIRKBRIDE.

[*From the Laboratories of the N. Y. State Department of Health, Albany.*]

For the purpose of ascertaining to what extent conditions of hypersusceptibility determine the character of pneumococcus lesions of the lung, series of experiments were made with a moderately virulent strain, and with an extremely virulent strain in its virulent state and after artificial attenuation. Rabbits were inoculated intravenously for purposes of sensitization with .1–15 c.c. pneumococcus filtrates or dead cells and then after two weeks injected tracheally with 1. c.c. live cultures. The animals surviving 48 hours were killed. Microscopic sections were made of all lungs.

In these experiments with attempted active sensitization none of the animals developed symptoms resembling anaphylactic shock nor was the lung involvement definitely increased in any series of previously treated rabbits. Tracheal injection of the moderately virulent organisms, however, caused marked lesions in both sensitized and unsensitized control rabbits.

In experiments with attempted passive sensitization, mixtures of 1 c.c. virulent or attenuated live cultures and .1 c.c. or .5 c.c. sera from normal or immunized rabbits when injected tracheally failed to incite uniformly extensive lesions in any series of animals though the proportion developing diffuse involvement was greater than in the previous experiments with active sensitization. Sudden paroxysms, similar to those of fatal anaphylactic shock were observed about twenty-four hours after tracheal injection in practically all the animals of two or three experiments. But these paroxysms were not associated with extensive lesions of the lung because in a number of the rabbits no characteristic exudative pneumonias were found, although the lungs were almost invariably deeply conjested.

While a hypersensitive state probably takes some part in the inception of the infection, these experiments indicate that the subsequent exudative lobar involvement is essentially a progressive and cumulative process.

116 (1048)

The nitrogen distribution of some feedstuffs and cereals.

By **J. F. BREWSTER** and **C. L. ALSBERG.**

[*From the Department of Agriculture, Washington, D. C.*]

The importance of knowing the amino acid content of feedstuffs has led the authors to apply Van Slyke's method[1] for the analysis of proteins direct, without previous isolation of the proteins themselves. The fine-ground and well-mixed material is weighed off in amount equivalent to 2–3 grams protein (estimated from the N-content) and completely hydrolyzed with 20 per cent. hydrochloric acid. Thereafter the method of Van Slyke is followed.

Analyses of corn, corn germ, cottonseed flour, kafir corn, tomato seed (pressed) and peat have been completed, results in duplicate agreeing well. The authors have had difficulty in accounting for the sulphur of the protein, the results for cystin being lower than was expected. This difficulty has been experienced by others and it is generally believed that if the cystin grouping be present, it is decomposed on hydrolysis and the sulphur changed to a form not precipitated by phosphotungstic acid with the cystin fraction. It is also conceded that sulphur exists in protein in other than the cystin grouping.

The results show Kafir corn and tomato seed meal to be lacking in histidin. Qualitative tests for tryptophan are positive for tomato seed, positive but slight for Kafir corn. Osborne and Clapp[2] found tryptophan and lysin, 2.93 per cent. in glutelin extracted from corn by weak alkali. The same investigators found neither lysin or tryptophan in zein of corn. Osborne's feeding experiments with cottonseed globulin show this protein to be satis-

[1] *Jour. Biol. Chem.*, X, 15. 1911.

[2] *Amer. Journal of Physiology*, **20**, 477. 1907.

factory for maintenance and growth. Lysin and tryptophan are both present. Other experiments by Osborne and Mendel indicate that lysin and tryptophan in the diet are both necessary for growth. If lysin be present without tryptophan maintenance is secured, but not growth. The writers found lysin N in both corn and cotton seed. The qualitative tests for tryptophan were positive. Unfortunately the determination of tryptophan by hydrolysis with acids has never yielded satisfactory results, it being thought that the tryptophan complex is broken down.

117 (1049)

The distribution of blood in shock.

By H. H. JANEWAY and HOLMES C. JACKSON.

[*From the Department of Physiology, University and Bellevue Hospital Medical College.*]

In a recent communication we have shown that the essential factor of shock is a disturbance in the normal distribution of the blood. This disturbance is of such a character that the normal quota upon the arterial side of the circulation is diminished and this diminution is maintained so that, as a consequence, even after the original cause of the disturbed distribution of the blood, whether of a mechanical, toxic or inhibitory nature, is removed the abnormal diminution of the blood upon the arterial side of the circulation not only persists but, in fatal cases, progresses from local peripheral causes alone until death occurs.

The reality and nature of these local factors in the production of shock is made clearest in that form of shock which is produced by mechanical means alone, because in shock created in this manner no other factor can enter except the consequences of a primary disturbance of the normal distribution of the blood.

The mechanical means which we adopted for the production of shock was that used for the reduction of blood pressure when testing out the shock-producing effect of trauma to the peripheral sensory nerves. It consisted in partially occluding the inferior vena cava within the chest by passing a thread around the vein and drawing out the two ends through the incision in the wall of

the thorax. By the degree of tension exerted on this thread, the amount of blood passing from the veins to the arterial side of the circulation could be accurately controlled and, in consequence, the blood pressure.

It was found that a two-hour period of reduction of the arterial blood pressure to from 30 to 40 mm. of Hg was, with few exceptions, fatal within the next eighteen hours, even though there might be a rise of arterial blood pressure to nearly the normal height for a period of three to four hours after the release of the ligature around the inferior vena cava. Manometric tracings of the systemic and the portal venous pressures showed an immediate rise in the venous blood pressure within these veins, following the occlusion of the inferior vena cava. As the experiment continued, there was a gradual fall in the pressures.

Volumetric tracings of the intestinal loops showed regularly a fall in the volume of the intestines during the period of occlusion. In the majority of the experiments, for a short time during the beginning of the period of occlusion there was a rise in the volume of the intestines. This was succeeded by a steady fall, which was maintained until a terminal stage when a very extreme condition of shock was reached, in which the volume of the intestine would show a small terminal increase.

Volumetric tracings of the liver, however, showed a consistent increase in the volume of this organ to a late stage in shock. The volume of the liver showed an increase relative to that of the intestines. It would decrease in size at the time of the terminal increase in volume of the intestines; and we attributed the terminal increase in volume of the intestines as being due simply to a draining away of the blood sequestrated in the liver by tissues in the intestines absolutely devoid of tone.

During the period when the progressive fall in the volume of the intestines is well instituted, the volume of the intestines and also of the liver shows a marked dependence upon the arterial blood pressure; whereas in the normal animal at the start of the experiment a tightening of the ligature around the inferior vena cava and the production of a rise in this manner of the portal venous pressure caused an increase also in the volume of the intestines. Later in the experiment, a similarly produced increase

of portal venous pressure showed a diminution of the volume of the intestines. In other words, the volume of the intestines during shock varied directly with arterial blood pressure, irrespective of increase or decrease in the portal venous pressure.

This, so to speak, inverse relation of the volume of the intestine can only be explained by recognizing that under such conditions of lowered blood pressure so little blood is supplied by the arterial side of the circulation that the effect of still further cutting down the arterial supply produces a greater effect upon the volume of the gut than the increased intravenous pressure. It must mean that the combined sectional area of the arterioles is already small.

These results confirm by another method of experimentation the conclusions of Mann, and of Morison and Hooker, and the failure in shock of venopressor mechanism, previously described by Henderson. Although we do not agree with Henderson's explanation of the cause of the failure of the venopressor mechanism, yet we entirely agree with the importance which he has ascribed to this mechanism. Our own experiments not only confirm the failure of the venopressor mechanism in shock but indicate the extent of this failure and the factors upon which it depends. We can see no other factor which can be responsible for the continued fall of blood pressure, after the period of partial occlusion of the inferior vena cava, than merely the effect of the mechanical distention of increased intravascular pressure upon the capillaries and small venules of regions draining into the inferior vena cava, and believe that this conclusion is emphasized by the comparatively high level to which the arterial blood pressure returns after the release of the ligature.

Of all parts of the vascular system, the capillaries and small venules are least capable of resisting the effects of increased intravascular pressure. The combined sectional area of the capillaries is very much greater than that of either the arterioles or the venules. Any increase in the capillary bed, even to a small extent, must, therefore, profoundly affect the general blood pressure. It is certain that during the period of occlusion of the vena cava the low blood pressure is due to the retention of blood within these vessels. In our experiments there is certainly no special sequestration in the vessels of the small intestine. The

experiments indicate rather that there is a special sequestration of the blood in the capillaries of the liver, but further that the increase in size of the liver, coupled with the diminution in the size of the intestines, cannot alone account for the diminished arterial blood pressure.

The crucial factor concerns the fact that after the relief of the obstruction to the flow of blood through the inferior vena cava there occurs, even after a more or less complete restoration of the arterial blood pressure, a progressive fall until death. This progressive fall can only be a consequence of some change in the walls of the vessels primarily affected by the occlusion of the inferior vena cava, namely, the capillaries and small venules. It is quite obvious, inasmuch as the total amount of blood circulating is a constant quantity, that an over filling of the vessels on the venous side of the most peripherally situated vessels possessing a muscular wall must be accompanied by diminished total sectional area of the vessels on the arterial side of the last vessels possessing power of active resistance to the volume of blood contained in them. All experiments indicate that the lumen of the smaller arteries and arterioles are diminished. The pressure laws of vaso-motor adjustment under conditions of reduced arterial blood pressure, the comments of Henderson, the findings of Muns, the results of the perfusion experiments of Morison and Hooker, all indicate that the arterioles and smaller arteries possess a diminished lumen in shock. We have demonstrated that there is at least no greater response to the injections of adrenalin in shock than before shock has been induced. This fact explains the failure of any great increase in volume of the combined intra-abdominal organs in shock.

In other words, our experiments of mechanically induced shock indicate that a mechanical distension of a certain degree and length of time is able to cause an alteration of the normally present contractility of the capillaries; in other words, of their tone, in virtue of which they lose the power of emptying the increased quantity of blood which they contain through the heart into the arterial side of the circulation, a power which they still preserve after either shorter periods of over-distention or distention of lesser degrees.

In mechanical shock induced by obstruction to the venous return to the heart, the over-distention is due to a draining back of the blood within the capillaries. In inhibitory shock, the over-distention is due to the sudden discharge of blood at high pressure into the capillaries. In either case, the effect upon the capillary wall is the same, and shock would therefore consist in a general displacement of what might be termed a critical quantity of blood from the arterial to the capillary and venous side of the circulation, a displacement which is therefore accompanied by comparatively insignificant volumetric changes and dependent largely upon a loss of a normally existing tone in the walls of the small venules and capillaries.

118 (1050)

On the application of the Kjeldahl method of nitrogen determination to serological problems. (Preliminary note.)

By **BYRON W. BARSHINGER.** (By invitation.)

[*From the Department of Bacteriology and Immunity, Leland Stanford Jr. University.*]

Practically no variation in the nitrogen content of rabbit serum (centrifuged) is produced by the usual variations in temperature at which the blood sample (sealed) is kept during the initial separation of the serum. Sera separated in the incubator, ice chest and at room temperature are identical, within the limits of the experimental error.

An increase of as much as 100 per cent. in nitrogen content may be brought about by increasing the length of time the serum is allowed to stand in contact with the clot. This increase is most rapid and most pronounced in samples kept at incubator temperature.

Variations as great as 40 per cent. may be observed in different samples removed from the same rabbit at the same bleeding. Small consecutive samples drawn at five-minute intervals may show differences as great as 10 per cent.

Variations as great as 40 per cent. above or below the average may be observed in sera of normal rabbits of the same age, size and breed, kept and bled under identical conditions.

119 (1051)

Metabolism in the dog before and after splenectomy.

By SAMUEL GOLDSCHMIDT, PH.D. and R. M. PEARCE, M.D.

[*From the John Herr Musser Department of Research Medicine, University of Pennsylvania.*]

SUMMARY.

Four dogs in nitrogen equilibrium were studied as to total output of nitrogen in urine and feces, output of ammonia, creatin and creatinin in the urine, and iron and fat in the feces. In each a preliminary control period of seven days was followed by like periods at intervals after splenectomy varying from three days to three months.

In three of the four animals the removal of the spleen caused no change in nitrogen metabolism, fat utilization or iron elimination. Two of these animals showed no change in the blood picture and the third only a slight non-progressive anemia. A fourth animal which developed eventually a moderately severe anemia showed slight loss of weight, a disturbance of nitrogen balance and of creatin-creatinin partition and an increased elimination of iron.

The following conclusions are reached: (1) that the removal of the normal spleen in an animal which remains otherwise normal causes no disturbance of metabolism: (2) that when disturbances of metabolism occur they are in all probability to be explained by the anemia which frequently follows splenectomy and not by a disturbance of metabolism consequent upon the absence of the spleen.

120 (1052)

Coagulation in relation to the proteid constituents of the blood.

By ALFRED F. HESS and E. J. BANZHAF.

[*From the Board of Health Laboratories, New York City.*]

As is well known there is a rearrangement of the proteins of the blood in the course of immunization. The most notable

change is an increase of the globulins and a decrease of the albumins. Such being the case, it seemed of interest to ascertain whether these modifications affected the rate of coagulability of the blood. Accordingly, the blood of a number of horses which have been immunized for months or years for the purpose of obtaining antisera against diphtheria, tetanus, meningitis, etc., was investigated from this point of view. Oxalated plasma was employed in the coagulation tests. The accompanying table gives the results of this investigation, and shows that the coagulation-time remains fairly constant in spite of marked variations in the proteins, that it is a factor which is not readily disturbed.

Horse No.	Total Protein.	Euglobulin.	Pseudo-globulin.	Albumin.	Coagulation Time.
414	6.93	.78	2.74	3.27	14 min.
508	6.15	.30	3.58	2.15	14 "
536	7.49	.54	4.08	2.66	12 "
542	6.49	.60	3.61	2.15	14 "
566	7.22	.53	2.98	3.59	7 "
593	6.93	.53	3.07	3.21	12 "
596	7.20	.76	2.90	3.37	14 "
N. 1	7.17	.61	3.42	2.97	12 "
N. 2	6.70	.48	3.05	2.98	15 "

121 (1053)

Inhibition of sodium oleate hemolysis and toxicity by cholesterin.

By OSKAR KLOTZ and MAY E. BOTHWELL.

[*From the Pathological Laboratories, University of Pittsburgh, Pittsburgh, Pa.*]

The hemolytic quality of soap solutions and particularly of sodium oleate has been studied by a number of investigators (Sachs, Meyer, Moore). Meyerstein later showed that the oleate hemolysis could be inhibited by lipoids, cholesterin, serum and organ extracts. Sodium stearate and palmitate are less active than the oleate. Moore has shown that the laking qualities of the soaps are in proportion to the unsaturated bonds of the fatty acids and that by iodine saturation can be inhibited.

The toxicity of soaps was studied by Munk who found that the quantity equal to 0.11 to 0.13 gram oleic acid per kilo body

weight killed rabbits. In his experiments he introduced these quantities very slowly. The heart action was depressed, but continued longer than the respiratory function.

We have given rabbits sodium oleate intravenously. A 5 per cent. solution of anhydrous sodium oleate (Merck) in normal saline was used. The soap solution was injected into the ear veins in a single and rapidly given dose. Doses of 0.1 sodium oleate per kilo appeared very irritating, the muscles of the extremities were thrown into spastic contractions and the animal had convulsive seizures. The ill effects lasted for a minute and a half when the animal would show great depression with rapid breathing. The muscles then became quite limp; within an hour the animal was fully recovered. Doses of 0.13 gram per kilo weight were fatal. These animals would sometimes enter a convulsive seizure before the injection was completely made. The blood of these animals after death was not perceptibly laked and it would appear that in the animal body the quality of laking and that of toxicity were separate. When, however, the solution of sodium oleate was mixed with an equal quantity of cholesterin the toxic qualities were inhibited. This cholesterin sodium oleate mixture was prepared by adding 5 per cent. cholesterin to a previously prepared 5 per cent. solution of sodium oleate in normal saline, and heating in a water bath for several hours. A milky and permanent emulsion was thus obtained which was found to contain no free cholesterin but was filled with great numbers of anisotropic bodies. These bodies are probably cholesterin-sodium-oleate compounds and are not the pure cholesterin esters described by others. This emulsion may be inoculated intravenously in doses containing double the quantity of the lethal sodium oleate. Irritating effects were still observed in spastic muscular contractions but there were transient. The emulsion inoculated intraperitoneally produced some inflammatory reaction with slight fibrin exudate. A single intravenous dose led to no permanent injury in the animal, but repeated inoculations every second day, led to much wasting, so that one animal in a period of twelve days lost 900 grams. Such animals when set at rest rapidly recovered. It is possible that the toxicity of the soap solution may be still further masked by increasing the cholesterin

to saturation. In this state, however, the compound is very gelatinous and hard to handle, while the addition of water for further dilution again leads to dissociation products.

Animals treated with the cholesterin sodium oleate mixture show no evidence of excretion of these substances in the urine. The compound readily circulates in the blood and is not filtered out by the capillaries. The lungs are quite free from change. We have noted, however, that frozen sections of formalin-fixed tissue showed anisotropic globules and an unusual amount of (?) cholesterin spicules in the liver parenchyma. The liver appeared quite yellow and fatty but the fat did not exist as the coarse globular fat of fatty infiltration. In these experiments we did not find the enlarged fatty adrenals as were present in another series in which the cholesterin materials were fed to the animals. The fate of the cholesterin and soaps has up to the present time not been determined.

The same cholesterin sodium oleate emulsion was used to demonstrate the inhibitory qualities of cholesterin upon soap hemolysis. It was found that 0.05 c.c. of a 5 per cent. solution of sodium oleate would hemolyze 1 c.c. of a 1 per cent. suspension of human blood cells in less than 18 hours at room temperature. On the other hand, 1.2 c.c. of the cholesterin sodium oleate compound did not hemolyze a similar quantity of blood. It was likewise found that the addition of normal serum to any mixture of sodium oleate and cholesterin still further inhibited the hemolysis and toxicity of the soap.

It is quite easy to prepare solutions of soap containing different quantities of cholesterin and by this means, observe the inhibitory influences of this substance. We have found that the 5 per cent. solution of sodium oleate in saline with the addition of 5 per cent. pure cholesterin is the most useful for study and is easily handled. The histological changes in tissues resulting from abnormal quantities of fluid cholesterin compounds will be reported upon later. By this combination of soap and cholesterin we have a means of introducing this otherwise inert substance in a fluid state which is assimilable.

122 (1054)

Studies in thyroid transplantation.

I. DATA RELATIVE TO THE PROBLEM OF SECRETORY NERVES.

By **O. T. MANLEY** and **DAVID MARINE.**

[*From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University, Cleveland.*]

During the past two years we have utilized the method of thyroid transplantation in rabbits in the attempt to get further data concerning certain questions in the physiology and pathology of this tissue. One of these questions is that of the necessity or not of specific secretory nerves to the gland. The observations of Anderson, Berkeley and Rhinehart have shown that in the thyroid both vessels and gland cells are abundantly supplied with nerve fibers. Stewart, Francois Frank and others have demonstrated the richness of the vasoconstrictor nerve supply, and Von Cyon demonstrated the presence of vasodilator fibers, both sets of fibers for the most part reaching the gland through the superior laryngeal nerves. More recently Asher and Flack and Ossokin have published physiological evidence which they think supports the view that the gland is under the control of secretory nerves, and Beebe and his associates have found that prolonged stimulation of the thyroid nerves causes a slight reduction in the iodin content which they interpret as indicating the presence of secretory nerves.

The method of transplantation eliminates many of the physiological and technical difficulties and objections of the acute experiments.

It has been found that under certain conditions thyroid tissue may be readily transplanted in widely separated parts of the body, as for example in the adrenal, ovary, subperitoneal tissues, muscle, subcutaneous fascia of the neck, chest and abdomen, and also, though with more difficulty, in the spleen and bone marrow. By transplanting and removing a sufficient amount of the main gland, care being taken to avoid all contact with iodin, we have always obtained compensatory hyperplasia of the remaining

stump, and in addition a simultaneous and similar degree of hyperplasia of any existing transplants independent of their location. Thus we have seen such reactions in ovarian, adrenal and subcutaneous transplants of the chest, neck and abdomen.

Now, if one gives very small doses of some idoin-containing substance, whether by mouth or by the use of a little tincture of iodin as in skin sterilization, involution promptly occurs in from two to three weeks which effects the transplants irrespective of their location in the same way as the main thyroid gland stump is effected. We have seen no exception to this except in cases where the total amount of thyroid tissue was below the level at which iodin will protect against thyroid hyperplasia. Also if iodin is administered prior to or at the time of transplantation, no hyperplasia of either the original gland or transplants occurs until the effect of the iodin has fallen to the level of inducing an insufficiency. Likewise if iodin is administered following transplantation, no hyperplasia ordinarily occurs during the time of such administration. We have followed such thyroid transplants for as long as 271 days.

If now a large part of the transplanted thyroid tissue and of the original gland, thus involuted, is removed, the remaining thyroid transplants and the remaining portion of the stump undergo active hyperplasia for the second time. This is similar in all essentials to the effects seen in dogs following alternate partial thyroid removals and iodin administrations. There is evidence also that transplanted thyroid tissues function. We have observed four rabbits showing marked amelioration of the symptoms of operative myxedema associated with active hyperplasia of subcutaneous abdominal transplants.

In view therefore of the facts that (1) under favorable conditions thyroid tissue may "take" and grow in widely different parts of the body; (2) that such transplanted tissue undergoes hyperplasia simultaneously and is histologically identical with that of the original gland stump; (3) that iodin induces an involution alike in both the transplanted and non-transplanted tissue, we believe (*a*) that the thyroid may function as a true blood-vascular gland in that the stimuli which cause these hyperplasias may reach the gland cells through the blood stream and that

influences causing thyroid involution may be transmitted by the same means; (*b*) that while these observations do not affect the question of the existence of specific secretory fibers, they demonstrate that such fibers are not essential in order that thyroid tissue may exhibit the characteristic morphological and physiological. changes known to be associated with great variations in functional activity; (*c*) that these data emphasize the necessity for additional evidence on the question of specific secretory fibers for the thyroid.

123 (1055)

On the action of sodium chloride in the prevention of proteotoxin shock.

By **HANS ZINSSER, CHARLES C. LIEB** and **JAMES G. DWYER.**

[*From the Departments of Bacteriology and Pharmacology, College of Physicians and Surgeons, Columbia University, New York.*]

It was shown by Friedberger and Hartoch that guinea-pigs could be protected against anaphylactic shock by an intravenous injection of hypertonic salt solution immediately preceding the toxic dose of antigen. That this protection is not due, as Friedberger and Hartoch claimed, to the inhibitory action of the salt on the alexin was demonstrated by Ritz, who found that an injection of salt also exerted protective action in animals injected with proteotoxins (the anaphylatoxins of Friedberger).

Dale concluded that the protection afforded by sodium chloride against acute anaphylaxis was due to the decreased irritability of the smooth muscle. He found that if the uterus of a sensitized guinea-pig were suspended in hypertonic salt solution, the addition of the antigen no longer caused the usual anaphylactic reaction. Other stimulating substances, like pilocarpine and pituitary extract, also failed to produce their typical stimulation provided that the uterus was bathed in hypertonic salt solution.

It is the object of the present investigation to show that, when a preliminary injection of salt protects against proteotoxin shock, the absence of reaction is due to the lessened irritability of smooth muscle.

In the first place, it was necessary to confirm, if possible, the

observations of Ritz. It must be remembered that, as Friedberger and Hartoch pointed out, the protective action of salt is a limited one and if the amount of antigen given at the second injection or if the amount of proteotoxin used is much above the minimal fatal dose, the poisoning is so acute and powerful that the protective effects of the salt are entirely masked. We had considerable difficulty at first in obtaining satisfactory experiments because of our failure to appreciate this relation, but when the toxic dose did not materially exceed the minimal fatal dose there was no difficulty in determining the protective effect of salt in guinea-pigs injected with proteotoxin. Preliminary tests showed that guinea-pigs ranging in weight from 165 to 200 grams could withstand, without serious effects, the injection of 1.5 c.c. of 30 per cent. salt solution into the external jugular vein. The blood oozing from the injection wound was a bright brick red. This striking change in color can not at present be explained. The salt solution must be injected very slowly, and we allowed from 1 to 12 minutes for its introduction. An interval of 2 minutes was allowed between the injections of the salt and the proteotoxin. Though this interval may not be absolutely necessary our most successful experiments were obtained when it was observed. The following three experiments are examples of the striking protective action exerted by the sodium chloride.

EXPERIMENT I.

Injections were made into the jugular veins; usually the salt solution was injected at a point close to the maxilla, a ligature applied and the proteotoxin injected proximally into the same vein. The injections of salt were carried out slowly, from one to one and a half minutes taken for the introduction of one cubic centimeter.

From these experiments it is plain that the toxic action of the proteotoxin (anaphylatoxin) is prevented by the immediately preceding injection of enough sodium chloride to render the blood of the animal hypertonic.

Having confirmed the experiments of Ritz it was next necessary to determine the mechanism of this protection.

It is well known that during anaphylactic shock violent con-

No.	Weight.	Salt, C.c.	Interval, Min.	Amount of Proteotoxin, C.c.	Result.
1.	185	—	—	2.5	Typical death in 3 minutes.
2.	185	—	—	2	Typical death in 3 minutes.
3.	185	—	—	1.5	Slight symptoms–recovers quickly.
4.	170	1.5	2	2	Very slight symptoms at first, gradually worse for 2½ minutes. Falls to side—then recovers.
5.	170	—	—	2	Typical death in 2½ minutes.
6.	165	1.5	2	2	(Very slight loss of proteotoxin during injection.) Pig shows hardly any symptoms.
7.	165	1.5	2	2	Severe symptoms for one minute. Then gets better and is in good condition within five minutes.
8.	160	1.5	2	2	Incubation time of 45 seconds, then respiratory distress and retraction of head. Gradual recovery.
9.	160	—	—	2	No interval—immediate severe symptoms. Death in 3¼ minutes.

Time of injection of salt was 1 minute 30 seconds in the above.

EXPERIMENT II.

No.	Weight.	Salt, C.c.	Interval, Min.	Proteotoxin, C.c.	Result.
1.	195	—	—	2.5	Death in 3¼ minutes.
2.	200	—	—	2	Death in 3 minutes.
3.	210	—	—	2	Death in 4 minutes.
4.	195	1.5	2	2	Very sick. Recovers.
5.	190	1.5	2	2	Not very sick. Recovers quickly.
6.	200	1.5	2	2	Very sick. Slow recovery. In good condition in 5 minutes.
7.	190	1.5	2	2	Slightly sick. Recovers quickly.
8.	180	1.5	2	2	Very sick. Gradually recovers.
9.	205	—	—	2	Death in 4 minutes.
10.	205	—	—	2	Death in 3½ minutes.

EXPERIMENT III.

No.	Weight.	Salt, C.c.	Interval, Min.	Proteotoxin, C.c.	Result.
1.	225	—	—	3	Very sick. Gradual recovery.
2.	210	—	—	3	Death in 4 minutes.
3.	205	1.5	2	3	Slightly sick. Rapid recovery.
4.	200	1.5	2	3	Very sick. Gradual recovery.
5.	205	1.5	2	3	Slightly sick. Recovers.
6.	210	—	—	3	Death in 3¼ minutes.
7.	205	—	—	3	Death in 3 minutes.

tractions of certain smooth muscle groups occur. The experiments of Schultz, Dale, Weil, and others, have pointed to a definite parallelism between the irritability of smooth muscle and the condition of sensitiveness. Furthermore, Dale has shown that a hypertonic salt solution prevents the usual reaction of the uterus of a sensitized guinea-pig to antigen. It was therefore necessary for us to determine whether an increase in the tonicity of the fluid bathing the uterus would abolish the reaction of the organ to proteotoxin. In our experiments the uteri of virgin guinea-pigs were used. The animals were etherized and exsanguinated. The uterus was excised and one horn was suspended in a glass cylinder in such a manner that its contractions would be recorded on the smoked paper of a slowly moving kymograph.

On adding a little fresh guinea-pig serum to the Ringer's solution in which a uterus is suspended a powerful contraction immediately ensues. If a small amount of salt solution is now added a total inhibition of the uterine movements occurs and the organ slowly relaxes. On replacing this mixture with pure fresh Ringer's fluid the normal rhythm and tonus usually return. When serum and salt solution are added together no contraction occurs.

Similar changes take place when proteotoxin is added to the Ringer's solution bathing the uterus. The spasm which follows such an addition may be removed by the subsequent addition of enough salt to approximate the concentration likely to be found in a guinea-pig of 200 gm. after the injection of 1.5 c.c. of 30 per cent. sodium chloride. If the uterus is surrounded by such a hypertonic salt solution the addition of proteotoxin fails to produce a typical spasm.

Occasionally a powerful contraction occurs after washing a preparation which because of the presence of excess salt has not reacted to proteotoxin. The explanation of this late spasm seems to be as follows: When the proteotoxin-salt mixture is siphoned away a trace of the mixture remains in the vessel. When the pure Ringer's solution is run in the original mixture is greatly diluted. The small amount of proteotoxin still remaining is sufficient to send the uterus into spasm because the quantity of salt remaining is insufficient to lower the irritability of the muscle.

In these experiments it is apparent that in the presence of a

hypertonic solution the uterus no longer reacts to serum or to proteotoxin.

The absence of reaction is due to a lessened irritability of the smooth muscle. Since the uterus is a typical example of a smooth muscle organ, it is very likely that all smooth muscle fails to react to proteotoxin when it is bathed in hypertonic solution. Such a decrease in irritability of smooth muscle will explain the protection against proteotoxin which an intravenous injection of concentrated salt solution affords.

124 (1056)

Clinical and experimental studies in chemotherapy with ethylhydrocuprein in measles, scarlet fever and other infections.

By ARTHUR D. HIRSCHFELDER and FREDERIC H. SCHLUTZ.

[*From the Department of Pharmacology and the Department of Medicine, Division of Pediatrics, University of Minnesota.*]

Morgenroth and his collaborators have demonstrated the prophylactic and curative and prophylactic powers of ethylhydrocuprein, a quinin derivative, in pneumococcus septicemia in mice.

The writers have given ethylhydrocuprein hydrochloride in doses of 0.1 to 0.5 G. three times a day by mouth to 7 cases of scarlet fever whose fever then had an average duration of 8.9 days as compared with 7.4 in 7 untreated cases who came under the same conditions in the same epidemic. In eleven unselected cases of measles, however, treated with the same drug, the average duration was 4.3 days as compared with an average duration of 7.9 days in ten untreated cases. One child who received the drug at the onset of symptoms, however, had an illness of 5 days' duration in spite of the early treatment.

The above experience seems to warrant the clinical use of ethylhydrocuprein in the treatment of measles, but not in scarlet fever.

Negative results with ethylhydrocuprein were obtained in experimental rabies and experimental vaccinia, also in trachoma.

125 (1057)

Tumor inoculation into the eye of an alien species.

By WM. H. WOGLOM, M.D.

[*From the George Crocker Special Research Fund, Columbia University, F. C. Wood, Director.*]

In recent articles Keysser[1] and his associate Hegner[2] have reported the successful inoculation of carcinomata and sarcomata from man and from the mouse into the vitreous humor of rats, an outcome which they ascribe to the absence of protective substances in the eye and to the indifferent character of its proteins. The tumors were injected in the form of a fine emulsion, the bulb being entered on its posterior aspect in order to avoid hemorrhage with the consequent entry of protective bodies from the blood stream.

Repetition of the experiment does not substantiate these claims. A few drops of a fine emulsion of Crocker Fund carcinoma No. 180 in Ringer's solution were injected under ether anesthesia into the eyes of rats, and a similar amount of the same emulsion into the eyes of normal mice to serve as controls; no hemorrhage occurred during the operation. The extreme proliferative capacity of this growth is shown by the fact that forty-nine mice out of fifty-four which survived for more than three weeks developed tumors from 0.5 to 1.5 cm. in diameter, while only five were negative. Since this approaches very closely the outcome of subcutaneous inoculation, the eye, as such, is not an unfavorable site for the growth of this neoplasm. Among eighty-three rats, however, none developed tumors, although thirty-five lived more than forty-two days after injection and eight as long as seventy-one days; hence, racial resistance protects the eye in common with the rest of the body. These findings were confirmed by microscopic examination of serial sections of the inoculated eyes.

[1] *Ztschr. f. Chemotherapie*, Originale, 1914, I, 188.

[2] *Münch. med. Wchnschr.*, 1913, LX, 2722.

126 (1058)

The excretion of sugars by the kidney.

By GEORGE PEIRCE and NORMAN M. KEITH.

[*From the James Buchanan Brady Urological Institute of Johns Hopkins University and Hospital.*]

In studying the excretion of any substance by the kidney there are at first glance three separate things to be considered.

First, the passage from the blood into the kidney cell; second, the transit through the cell substance; and third, the passage from the cell into the lumen of the glomerulus or tubule. It is obvious that if the transfer through either cell boundary is impossible that none of the substance can be excreted, and it is also obvious that if anything prevents the passage through the cell substance itself that the kidney will appear impermeable.

In considering the passage of glucose through the body of the cell there are two well-known facts to be borne in mind that so far as we know have not received sufficient attention in this connection. The first is that the kidney uses a relatively large amount of oxygen and the second is that glucose is one of the main sources of energy for the body in general. It is therefore very probable that the kidney normally oxidizes a certain amount of glucose. Hence, even if both cell boundaries are permeable for glucose not all the sugar that gets into the cell will reach the lumen of the tubule. Normally only the minutest trace of sugar is present in the urine, whereas if the blood sugar rises beyond a certain level some will appear. Although it is true that in certain cases of diabetes there may be only a very slight hyperglycemia yet it is in the main true that glycosuria is dependent on a more or less pronounced rise in the percentage of sugar in the blood. Many hypotheses have been advanced to account for this so-called threshold phenomenon and I hope you will pardon me for dismissing them with the statement that none of them are generally accepted. It has seemed to us that the true explanation lies along the lines indicated above. The sugar normally gains entrance into the kidney cells in proportion to its concentration

in the blood. During its passage through the cell some of it is oxidized and if not too much has gotten in all will be oxidized and none appear in the urine.

In testing out this hypothesis we have referred to published figures for the concentration of various substances in the blood and urine and have also made some experiments of our own. We have found that very roughly speaking a dog of 10 k. body weight with a blood sugar content of .1 per cent. should excrete about .7 g. sugar per hour if the kidney were completely permeable and secreting freely. During marked diuresis Barcroft and Brodie[1] found that about 660 c.c. of oxygen would be required by the dog's kidneys for the same period. 0.7 g. of sugar requires 520 c.c. of oxygen for complete oxidation to CO_2 and water. The correspondence is fairly close.

We have also used published figures for the blood flow through the kidneys and have estimated that the sugar content of the renal vein should be about 80–90 per cent. of the sugar content of the renal artery if the kidney is completely permeable. We obtained simultaneous samples of the blood from the femoral artery and renal vein and found in five experiments a difference of 10–15 per cent., in three experiments no difference and in two a slightly higher content in the renal vein than in the artery. We drew 10 c.c. samples and analyzed the oxalated plasma by Shaffer's method. In only one of our experiments was any glucose found in the urine and then only a trace. We are engaged at present in trying to improve the analytical methods and will not go into further details.

We have tested a number of sugars and the indications are at present that only the sugars that are oxidized by the body will show this so-called threshold phenomenon. We believe we are justified in making the following statement: If the kidney is permeable for a sugar when and only when its concentration in the blood rises beyond a certain level, that sugar is oxidized by the kidney.[2]

[1] Barcroft and Brodie, *Journal Physiol.*, 33, 52 (1905–06).

[2] We even venture to suggest on purely theoretical grounds the following: If the kidney is permeable for any substance when and only when its concentration in the blood rises beyond a certain level, that substance is metabolized by the kidney.

127 (1059)

The inhibitory effect of adrenalin upon the sphincter of the pupil.

By DON R. JOSEPH.

[*From the Department of Physiology, Saint Louis University.*]

The sphincter muscle from the eyes of cattle, sheep and hogs was tested as quickly as possible after death. Two methods were used: (*a*) A strip, containing the sphincter, was cut from the pupillary border of the iris, connected with a lever and kept in a bath of either saline, Ringer's solution or aqueous humor, at 38 to 40 degrees Centigrade—in some cases with oxygen streaming through. (*b*) In other cases the sphincter was only partly excised, but connected with the registering apparatus in such a way that contraction or relaxation of the sphincter alone could affect the lever. In these experiments the iris was kept in an enclosed, warmed, air chamber and adrenalin dropped upon it from a pipette at the time of the test. The 1 : 1,000 Parke Davis solution was used.

Over 50 experiments are included in this report. Adrenalin produced, practically without exception, a relaxation of the sphincter. This was true for each of the three species of animals tested. The relaxation began promptly and at first was rapid so that the lever traced very nearly a vertical line on the drum. Later the rate of relaxation slowly decreased but in most cases continued until it seemed to be maximal. No recovery was seen even when the adrenalin bath was replaced with a fresh non-adrenalin-containing bath. That the sphincter was still irritable, however, was demonstrated by the addition of physostigmin, when a good contraction usually resulted.

This inhibitory effect of adrenalin indicates that the cervical sympathetic supplies inhibitory nerve fibers to the sphincter muscle of the iris.

128 (1060)

On the mechanism of pneumococcic immunity. (Preliminary note.)

By **KAY J. KITAGAWA.** (By invitation.)

[*From the Department of Bacteriology and Immunity, Leland Stanford Jr. University.*]

Normal rabbits.—First generation pneumococci injected intravenously into normal rabbits decrease in number in the circulating blood during the first thirty minutes. The pneumococcic count (plate method) at the end of thirty minutes is usually about 25 per cent. of the initial count. After thirty minutes the number either slowly increases or slowly decreases depending upon the dosage and virulence of the organism injected.

Immune rabbits.—First generation pneumococci injected intravenously into actively immunized rabbits generally disappear with great rapidity from the circulating blood. By the end of ten minutes the blood is usually sterile.

Little or no decrease in the pneumococcic count is observed in samples of blood isolated from the general circulation between ligatures placed about a blood vessel. Even at the end of an hour the count in the isolated blood sample may be nearly as great as the initial count at the time the ligatures were closed.

From this it is evident that the rapid disappearance of the pneumococci from the circulating blood of actively immunized rabbits is not due to a destruction of the pneumococci by the plasma or leucocytes, but to their mechanical removal or destruction by the fixed tissues through which the blood circulates.

129 (1061)

On sub-muscular skin transplantations. (Preliminary note.)

By HARRY CARSON COE. (By invitation.)

[*From the Department of Bacteriology and Immunity, Leland Stanford Jr. University.*]

Skin transplantations on smaller laboratory animals are usually unsuccessful due to difficulties of bandaging and immobilization. As a preliminary to certain immunity studies an operation has been devised to avoid these difficulties, the animals' own tissues being used as a means of immobilization and surgical dressing.

On guinea-pigs, for example, an incision is made in the mid-dorsal line and the skin and superficial muscles resected. The skin graft is placed in the sub-muscular pocket thus formed and fastened to the periostium of the ribs with silk sutures. The resected tissues are drawn up over the graft and the dorsal incision permanently closed.

About a week later, the superficial tissues are resected over the graft, and the edges of the resection wound sewed to the graft with silk sutures. The exposed graft is protected for a week or two with a light dressing of silver foil and cotton.

The results of the operation are good, so far as the initial union of tissues is concerned.

130 (1062)

On the reaction of the anaphylactic uterus in situ. (Preliminary note.)

By WILLIAM H. MOORE and YOSHIO KUSAMA. (By invitation.)

[*From the Department of Bacteriology and Immunity, Leland Stanford Jr. University.*]

Strips of the anaphylactic guinea-pig uterus contract strongly when tested with the foreign proteid toward which the guinea-pig is sensitive. Our attempts thus far to record similar contractions by applying the proteid to the uterus *in situ* have been unsuccessful.

From this it would seem that the reaction of the anaphylactic uterus while still supplied with normal nerve and blood elements is different from its reaction when isolated from the rest of the body.

131 (1063)

Effect of lead salts and of the nitrites upon the movements of the intestines.

By A. D. HIRSCHFELDER, J. M. ARNSON, R. HOUDE, G. M. MERKERT and M. J. SHAPIRO.

[*From the Department of Pharmacology of the University of Minnesota.*]

Riegel (1875) and J. Pal (Die Gefässkrisen, 1906) suggested the use of amylnitrite for the control of pain in lead colic and in the gastric crises of tabes dorsalis, believing that the fall of blood pressure sufficed to bring about diminution in these symptoms.

The present series of experiments was undertaken in order to determine whether the nitrites might not act by causing relaxation of a spastic condition of the intestinal walls. The experiments were carried out on rabbits whose intestinal movements were observed through a large window in the abdominal wall, which was closed from the outside air by inserting a crystallizing dish 10 cm. in diameter. The sides of the crystallizing dish were coated with thick beeswax and the window was held in place by fixing the abdominal walls around it with a purse string suture. The animals were lightly anæsthetized with ether.

Injection of 5 mg. lead acetate per kg. immediately caused the onset of intense peristaltic movements which seemed to be due to stimulation of the preganglionic synapse, since they were abolished by injection of nicotin or by painting nicotin upon the intestine, but were not affected by extirpation of the spinal cord and section of the vagi. As was suspected from the clinical results reported by Riegal and Pal, this peristalsis could be inhibited by inhalation of amylnitrite, by placing two drops of nitroglycerin upon the tongue or by the injection of 80-100 mg. per kg. sodium nitrite. The effects of the two former drugs were most marked, though the effects of the latter were more prolonged.

Atropin, either locally or intravenously, also inhibited the peristalsis, as had been shown by Harnack.

The same effects were also obtained with the nitrites and with atropin when increased peristalsis was brought on by the local effect of heat, secured by placing warm water in the crystallizing dish window. The increased peristalsis resulting from this procedure was inhibited by amylnitrite, nitroglycerine and sodium nitrite, and atropin, exactly as was the lead peristalsis. Similar effects were obtained when the peristalsis was produced by direct faradization of the solar plexus which also was inhibited by these drugs.

These experiments establish the rôle of the nitrites as inhibitors of intestinal peristalsis, and furnish an experimental basis for the therapeutic results obtained by Riegel and Pal in lead colic, and by the latter also in the gastric crises of tabes, by the administration of amylnitrite; and they demonstrate that the mechanism in these cases is probably not merely the change in blood pressure but particularly the inhibition of intestinal spasm.

The results are quite uniform, sudden and striking enough to warrant its use as a class exercise in experimental pharmacology.

132 (1064)

Observations upon a rat sarcoma treated with emulsions of embryonic tissues. (Preliminary Report.)

By KENNETH TAYLOR, M.A., M.D. (By invitation.)

[*From the Department of Pharmacology, University of Minnesota, Minneapolis.*]

In view of the accepted value of total embryo emulsion as on immunizing agent against propagable tumors first demonstrated by Schöne (Munch. Med. Woch., 1906, LIII, 2517) and later used successfully by many other investigators, the following notes on the influence of special embryonic tissues and of placenta on established rat sarcoma seem of sufficient interest to be reported.

The tumor used in these experiments was a sarcoma kindly supplied the laboratory by Dr. Loeb. During the period covered by the investigations it showed the following biological characteristics:

It was readily inoculated by direct subcutaneous transplantation of small intact fragments, giving by this method successful transplants in 93.2 per cent. of albino rats used in five separate operations. A palpable tumor usually developed in about six days, growing progressively and rapidly and having an average diameter of 30 mm. at the end of seven weeks. It usually invaded the skin and body wall only in the late stages of its growth. The average life of the animals after the inoculation was about ten weeks. No metastases were found on macroscopic post mortem examination. Retrogressions to complete disappearance occurred in six out of the fifty controls used in these experiments (12 per cent.). These retrogressions occurred only in the tumors which remained under 12 mm. in diameter. Recurrences after retrogression were not observed.

The animals used were albino rats about two thirds grown, males and females in about equal numbers.

The treatment was conducted with normal salt emulsions of the thyroid, the spleen and the liver of rat embryos prepared under aseptic precautions and preserved in the ice-chest under toluol, and also with an extract of placenta with the attached uterus washed free of blood and prepared in a similar manner. The emulsions were injected subcutaneously three times a week, the dosage so regulated that each animal received in the course of twelve injections the emulsion of two complete thyroids, or two spleens, or two placenta, or one liver.

Treatment was begun in each case the twelfth day after inoculation with the tumor. As the experiments were carried on practically simultaneously, the same controls have been used for each series. Among them are included five rats treated with embryo spleen. The other control animals received no treatment.

The results of treatment are shown in the table below:

Treatment.	Number of Animals.	Retrogressions Number.	Per Cent.
CONTROLS	50	6	12
Fœtal thyroid	7	4	57.0
Fœtal liver	7	3	42.5
Placenta and uterus	7	2	28.5
Fœtal spleen	5	0	0

It may be of interest to note that the size of the tumors which

did not retrogress in those animals treated with embryo thyroid, liver, or placenta, was at the end of seven weeks usually above the average size in untreated animals (average 40.3 mm. as against 30 mm. an increase in size of 34). In nearly every case, then, these treated tumors have shown a deviation from the normal growth of the controls.

The number of animals treated is obviously too small to permit definite conclusions to be drawn in the case of any tumor showing even a low percentage of retrogressions, but the results are, I believe, sufficiently marked to make it desirable to record them while more extensive tests are being carried out.

There appeared, however, to be an increased incidence of retrogressions in tumor-bearing rats after treatment with embryo thyroid, liver or placenta and uterus. Embryo spleen seemed to have little or no inhibitory action on the growth of the tumors. It seems probable that further analysis of the embryonic tissues may reveal a wide variation in the therapeutic value of different issues, and that special tissues may prove to be more effective against the growing tumors than the emulation of the whole embryo.

I wish to express my thanks to Dr. Arthur D. Hirschfelder, director of the Department of Pharmacology of the University of Minnesota, for his valuable criticism of my experiments.

(*Note by Dr. Hirschfelder.*) Since the deparutre of Dr. Taylor for Europe some months ago, all the transplants of this rat sarcoma both in our laboratory and in Dr. Loeb's, have undergone retrogression or failed to develop. This retrogression occurred only in tumors about two generations later than those of Dr. Taylor's experiments. The possibility therefore suggests itself that at the stage of Dr. Taylor's experiments the tumor, though of demonstrated virulence, may have been in a stage particularly favorable for therapeutic procedures; and these experiments are reported in the hope that they may be repeated with other tumors which are nearing, but have not yet reached the stage of spontaneous retrogression.

RECAPITULATION OF THE NAMES OF THE AUTHORS AND OF THE TITLES OF THE COMMUNICATIONS.

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Benedict, S. R.

959. [with **E. Osterberg.**] The influence of feeding upon acidosis in the phlorhizinized dog.

Bengis, R.

1029. See **Salant, William.**

Berg, W. N.

1019. A theory of internal disinfection with nascent formaldehyd.

Bergeim, O.

946. The origin of gastric hydrochloric acid.

947. Phospho-nuclease as related to phosphorus and calcium metabolism.

998. The influence of certain agents on the activity of phospho-nuclease.

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1053. See **Klotz, O.**

Braddock, W. H.

981. See **Butterfield, E. E.**

Brewster, J. F.

1048. [with **C. L. Alsberg.**] Nitrogen distribution of some feedstuffs and cereals.

Bronfenbrenner, J.

934. The proteolytic enzyme is not specific.

935. The Abderhalden reaction is not an adsorption phenomenon.

936. The Abderhalden test is rendered negative by the addition of serum antitrypsin.

937. The serum is the source of dialyzable substances.

963. Application of the serum-skin test to the diagnosis of pregnancy and different pathological conditions.

999. [with **M. J. Schlesinger.**] On the action of anesthesia in anaphylaxis.

1014. A new principle in isolation of spirochetes in pure culture.

1015. [with **K. M. Scott.**] The demonstration of tryptic digestion by an activated serum.

1031. See **Van Slyke, D. D.**
1044. See **Van Slyke, D. D.**

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1042. Inheritance of temperament.

Denzer, B. S.
1020. See **Weil, Richard.**

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994. See **Barber, W. H.**
1023. See **Barber, W. H.**

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942. [with **E. F. DuBois.**] The measurement of the surface area of adults.

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942. See **DuBois, D.**

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1055. See **Zinsser, H.**

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980. See **Lee, F. S.**

Erdmann, R.
968. A new culture medium for protozoa.

Feldstein, S.
1046. A method for studying the effect of serum upon tissues.

Field, C. W.
1024. See **Pfeiffer, J. A. F.**

Fine, M. S.
956. See **Myers, V. C.**
990. See **Chace, A. F.**

Garrison, P. E.
957. See **Siler, J. F.**

Gates, F. L.
970. [with **S. J. Meltzer.**] The influence of the intra-intestinal administration of magnesium sulphate upon the production of hyaline casts in dogs.

Gay, F. P.
1002. [with **H. T. Chickering.**] Concentration of the protective bodies in antipneumococcus serum by means of specific precipitation.

1063. [with **J. M. Arnson, R. Houde, G. M. Merkert M. J. Shapiro.**] Effect of lead salts and of nitrites upon the movements of the intestines.

Houde, R.

1063. See **Hirschfelder, A. D.**

Howland, J.

965. [with **W. McK. Marriott.**] Observations upon the so-called "food intoxication" of infants with especial reference to the alveolar air.

Jackson, H. C.

986. Reflex cardio-inhibition in conditions of lowered blood pressure and "shock."

1049. See **Janeway, H. H.**

Janeway, H. H.

984. The influence of nocuous stimuli in the production of shock and the failure of this influence to support the anoci theory of shock.

1049. [with **H. C. Jackson.**] The distribution of blood in "shock."

Jordan, H. E.

1033. The shape of the human red blood corpuscle.

Joseph, D. R.

964. See **Seelig, M. G.**

1016. The effect of adrenalin on the pupil after removal of the ciliary ganglion.

1059. The inhibitory effect of adrenalin upon the sphincter of the pupil.

Keith, N. M.

1058. See **Peirce, G.**

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1047. The effect of sensitization on pneumococcus lesions of the lobar type in rabbits.

Kitagawa, K. J.

1060. On the mechanism of pneumococci immunity.

Kleiner, I. S.

969. [with **S. J. Meltzer.**] The influence of depancreatization upon the state of glycaemia following the intravenous injection of dextrose in dogs.

Ott, Isaac.

961. [with **J. C. Scott.**] Note on action of corpus luteum upon mammary glands.

Painter, T. S.

973. The effect of carbon dioxide on the eggs of *Ascaris.*

Palmer, G. T.

1017. See **Winslow, C.-E. A.**

Pearce, R. M.

1051. See **Goldschmidt, S.**

Pearl, Raymond.

943. On the law relating milk flow to age in dairy cattle.

962. [with **J. W. Gowen.**] On the refractive index of the serum in a guinea-chicken hybrid.

Peirce, G.

1058. [with **N. M. Keith.**] The excretion of sugars by the kidney.

Pepper, O. H. Perry.

1041. [with **J. H. Austin.**] Studies of urinary and blood nitrogen curves after feeding in the dog.

Pfeiffer, J. A. F.

1024. [with **P. A. Kober** and **C. W. Field.**] Relation of euglobulin, total-globulin and total protein to Wassermann reaction.

Rasmussen, A. T.

991. See **Simpson, S.**

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975. The intra-uterine growth of infants, estimated by the weights of pre- and post-maturely born infants.

976. The post-natal loss of weight in infants and the compensatory over-growth which succeeds it.

977. [with **T. C. Burnett.**] The influence of the anterior lobe of the pituitary body upon the growth of carcinoma.

Rohdenburg, G. L.

1027. See **Bullock, F. D.**

EXECUTIVE PROCEEDINGS

Sixty-first Meeting.

Cornell University Medical College, October 21, 1914. President Lusk in the chair.

Members present: Atkinson, Auer, Beebe, Bronfenbrenner, Burrows, DuBois, Eggleston, Evans, Field, Fine, Gies, Githens, Goldfarb, Hartwell, Howe, Jackson, Kleiner, Lee, Lieb, Longcope, Lusk, MacDougal, Murlin, Myers, Pappenheimer, Pike, Rous, Scott, E. L., Teague, Senior, Sherman, Storey, Swift, Van Slyke, Wallace, Weil, Wiggers, Winslow.

Sixth Meeting.

Pacific Coast Branch.

San Francisco, California, October 7, 1914.

Members present: Cooke, Crawford, Dickson, Lucas, Ophüls, Robertson.

Sixty-second Meeting.

New York Post Graduate Medical School, November 18, 1914. President Lusk in the chair.

Members present: Benedict, S. R., Eggleston, Emerson, Ewing, E. M., Fine, Gies, Harris, Hess, Howe, Jackson, Kast, Kleiner, Lieb, Lusk, MacNeal, Mandel, A. R., Meltzer, Myers, Senior, Swift, Wallace, Weil.

Sixty-third Meeting.

Rockefeller Institute for Medical Research, December 16, 1914. President Lusk in the chair.

Members present: Auer, Cohn, DuBois, Gies, Githens, Harris, Hess, Howland, Jackson, Kleiner, Lusk, MacCallum, MacNeal, Murlin, Myers, Oppenheimer, Van Slyke, Wiggers.

Members elected: Olaf Bergeim, T. C. Burnett, J. A. Kolmer, S. S. Maxwell, Oscar Riddle, G. H. Whipple, W. C. Thro.

Resignations: F. G. Benedict and L. Hektoen.

Seventh Meeting.

Pacific Coast Branch.

San Francisco, California, December 2, 1914.
Members present: Crawford, Lucas, Ophüls, Robertson.

Sixty-fourth Meeting.

College of Physicians and Surgeons, January 20, 1915. President Lusk in the chair.

Members present: Auer, Burton-Opitz, Butterfield, Coca, DuBois, Eisenbrey, Emerson, Ewing, E. M. Ewing, J., Field, Fine, Gies, Githens, Greenwald, Hartwell, Howe, Jackson, Lee, Lieb, Loeb, J., Longcope, Lusk, Murlin, Myers, Norris, Oppenheimer, Pike, Scott, E. L., Swift, Terry, Van Slyke, Weil, Williams, H. B., Winslow.

Sixty-fifth Meeting (Twelfth Annual Meeting).

College of the City of New York, February 17, 1915. President Lusk in the chair.

Members present: Atkinson, Auer, Bailey, Bull, Draper, Ewing, E. M., Famulener, Fine, Githens, Goldfarb, Harris, Hess, Jackson, Kleiner, Lee, Levin, Lieb, Lusk, MacNeal, Meltzer, Murlin, Myers, Ringer, Rous, Scott, E. L., Scott, G. G., Senior, Simpson, Storey, Thro, Wiggers, Winslow.

The meeting was held at 4:30 P.M. and was followed by a dinner at 7:00 P.M. At the adjourned meeting after the dinner, various amendments to the Constitution and By-Laws were proposed to be voted upon at the March meeting.

Officers elected: President, Graham Lusk; Vice-President, G. N. Calkins; Treasurer, J. R. Murlin; Secretary, Holmes C. Jackson.

Eighth Meeting.

Pacific Coast Branch.

San Francisco, California, February 3, 1915.

Members present: Burnett, Cooke, Dixon, Gay, Lucas, Meyer, K. F., Ophüls, Swain, Whipple.

Sixty-sixth Meeting.

Pathological Department of Bellevue Hospital, March 17, 1915. President Lusk in the chair.

Members present: Auer, Bailey, Cole, R. L., Dunham, Ewing, E. M., Falk, Field, Gettler, Gies, Githens, Goldfarb, Greenwald, Harris, Hatcher, Hess, Howe, Jackson, Kleiner, Lusk, Meltzer, Myers, Norris, Pappenheimer, Rous, Sherman, Thro, Wallace, Wasteneys, Wiggers.

Amendments to the Constitution and By-Laws were adopted and these changes have been incorporated in the Constitution and By-Laws of the Society, see page 236.

Sixty-seventh Meeting.

University and Bellevue Hospital Medical College, April 21, 1915. President Lusk in the chair.

Members present: Benedict, Berg, Bull, Draper, Fine, Gies, Goldfarb, Hatcher, Hess, Jackson, Lusk, Mendel, Myers, V. C., Senior, Terry, Wallace, Weil, Winslow.

Members elected: P. A. Kober, D. J. Edwards, H. B. Lewis, Warren Coleman, Alfred Reginald Allen, O. H. Perry Pepper, E. L. Walker, Thomas Addis, W. H. Barber, O. E. White.

Resignation: F. F. Russell.

According to the revision of the Constitution the office of Treasurer was abolished and the present Treasurer automatically went out of office. At this meeting a special election to fill the office of Secretary-Treasurer was held and Holmes C. Jackson was elected to fill the office. W. J. Gies and J. Auer were elected as additional members of the Council.

Ninth Meeting.

Pacific Coast Branch.

San Francisco, California, April 7, 1915.

Members present: Burnett, Cooke, Crawford, Dixon, Gay, Meyer, Ophüls, Swain.

Sixty-eighth Meeting.

Columbia University, May 19, 1915. President Lusk in the chair.

Members present: Alsberg, Auer, Austin, Beebe, Bull, Davenport, Eisenbrey, Fine, Githens, Harris, Hess, Howe, Jackson, Kleiner, Lusk, Meltzer, Murlin, Myers, V. C., Oppenheimer, Ottenberg, Pepper, Peirce, Van Slyke, Wadsworth, Wasteneys.

Members elected: G. M. Baehr, F. S. Jones, V. L. Kellogg, Mary B. Kirkbride, R. A. Kocher, W. G. Lyle, W. C. Noble, A. Zingher.

Resignation: B. H. Buxton.

CONSTITUTION AND BY-LAWS.

CONSTITUTION.

[As adopted Feburary 25, 1903, and amended, April 20, 1904, May 24, 1905, February 21, 1906, April 18, 1906, May 22, 1907, and March 17, 1915.]

Article I. Name.

The name of this organization shall be the Society for Experimental Biology and Medicine.

Article II. Object.

The object of this Society shall be the cultivation of the experimental method of investigation in the sciences of biology and medicine.

This object shall be attained (a) by the holding of meetings at which original communications shall be presented; (b) by the publication of Proceedings.

Article III. Membership.

Section 1. *Eligibility.*—Any person who has accomplished a meritorious original investigation in biology or medicine by the experimental method shall be eligible to membership.

Section 2. *Forfeiture.*

Any member of this society who may consent to the use of his name in any way that would aid in increasing the sale of any patent medicine, proprietary food preparation, or any similar product **for which, in the opinion of the Council, inaccurate or misleading claims are made,** shall forfeit his membership.

Section 3. *Nomination and Election.*—*A.* Each candidate for membership must be nominated by three members.

B. After their eligibility has been determined by the council, nominees may be voted for at any meeting succeeding that at which their names were presented.

C. A three-fourths vote of the ballots cast shall elect.

Section 4. *Expulsion.*—Any member may be expelled by a three-fourths vote of the total membership.

ARTICLE IV. MEETINGS.

SECTION 1. *Time.*—The Society shall hold regular meetings at least once every two months during the academic year.

SECTION 2. *Annual Business.*—The first regular meeting of each calendar year shall be an annual business meeting.

SECTION 3. *Program.*—The programs of the meetings shall consist of (*A*) brief presentations, in elementary form, of the essential points of experimental investigations, preferably demonstrations of actual experiments; and (*B*) **of papers to be read by title.**

ARTICLE V. OFFICIALS.

SECTION 1. *Officers.*—**The Officers shall be a President, a Vice-president, and a Secretary-treasurer.**

They shall be elected from those members whose scientific work is conducted within the limits of Greater New York.

SECTION 2. *Council.*—**The council shall consist of the President, the Vice-president, the Secretary-treasurer and two members of the Society, one elected annually to serve two years. Ex-presidents of the Society shall be permanent members of the Council.**

SECTION 3. *Nomination and Election.*—*A.* Nominations of officers shall be made in the regular session immediately preceding the annual business meeting.

B. Election of officers shall be by ballot at the annual business meeting.

C. A plurality of the vote cast shall elect.

SECTION 4. *Term of Office.*—The term of office shall be one calendar year **except as specified above for the Council.**

SECTION 5. *Duties.*—*A.* The duties of the officers shall be such as usually devolve on them individually, and also collectively, as an executive committee.

B. The council shall promptly investigate and report its findings on the eligibility of candidates for membership and on the desirability of each candidate's election.

ARTICLE VI. FINANCIAL.

SECTION 1. *Dues.*—**The council shall have authority to fix the amount of the annual dues.**

SECTION 2. *Privileges of membership begin with payment of dues.* Candidates for membership, if elected, shall not be entitled to any of the privileges of membership before they pay the dues for the fiscal year in which their election occurs.

SECTION 3. *Penalty for non-payment of dues.* Members in arrears for dues for a period of three consecutive years shall thereupon forfeit their membership, but may be reinstated by the council.

ARTICLE VII. QUORUM.

Twenty members shall constitute a quorum for the transaction of business.

ARTICLE IX. BY-LAWS.

By-laws may be adopted at any meeting by a majority vote.

Article VIII. Local Branches.

Section 1. Formation.—Groups of members of the Society shall be allowed by special vote to form local branches, such branches to be designated by local names.

Section 2. Membership.—Only members of the Society as a whole, duly proposed and elected according to the Constitution, shall become members of the local branches.

Section 3. Programs and Publications.—The expense of such local meetings and the preparation of the programs shall be assumed by the local branches. The publication of their proceedings shall take place in the Proceedings of the Society.

ARTICLE X. AMENDMENTS.

SECTION 1. Proposed amendments of the constitution must be endorsed by at least three members, at a regular meeting, and may be voted on at a succeeding meeting.

SECTION 2. It shall be the duty of the secretary to give all members due notice of intended amendments.

SECTION 3. A two thirds vote of the total membership, or a unanimous vote of the members present, shall be required for the adoption of an amendment.

BY-LAWS.

Adopted February 25, 1903, and amended May 24, 1905, February 21, 1906, and March 17, 1915.

I. *Meetings.*—A. **Regular meetings shall be held on the third Wednesday of the months of October to May inclusive.**

B. Special meetings may be called by the council.

C. The meetings shall be opened at 8:30 P. M.; two hours shall be devoted to the reading of papers.

D. When possible the meetings shall take place in suitable laboratories.

II. Editorial Committee: The President shall appoint each year an editorial committee consisting of the Secretary-treasurer and two members of the Society. This committee shall have immediate supervision over the preparation of the program and discussion, shall devise rules governing the publication of papers in the Proceedings of the Society, and shall fix the price of the Proceedings to non-members.

III. Program: A. The first eight papers presented to the Secretary to be read in person shall constitute the scientific program for the meeting; all other reports shall be read by title or with the consent of the author shall be transferred to the program of the succeeding meeting.

B. Precedence on the program shall be given to non-resident members and to demonstrations.

C. No member shall be allowed to read more than one paper at each meeting unless in the event of lack of other material to fill the program.

D. Precedence shall be given, on each program, to communications which have not been presented before any other body and which have to do with investigations essentially experimental in character.

IV. *Regulation of Reports and Discussions.—A.* The time allowed for making individual communications, except demonstrations of experiments shall be restricted to ten minutes.

B. Not more than five minutes shall be allowed to a member for the discussion of any communication.

V. Order of Procedure, to be followed at the regular meetings.

A. Call to order.
B. Reading of minutes.
C. Report of council.
D. Reports of committees.
E. Unfinished business.
F. Election of members.
G. Nominations for membership.
H. New business.
I. Scientific program.
J. Adjournment.

REGISTER OF NAMES AND ADDRESSES OF THE MEMBERS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE

ABBOTT, ALEXANDER C.....University of Pennsylvania.
ABEL, JOHN J.....Johns Hopkins University.
ADAMI, J. GEORGE.....McGill University, Montreal.
ADDIS, THOMAS.....Lane Hospital, San Francisco.
ADLER, HERMAN M.....Psychopathic Hospital, 74 Fenwood Road, Boston.
ADLER, ISAAC.....New York Polyclinic Medical School.
ALLEN, A. REGINALD.....University of Pennsylvania.
ALSBERG, CARL.....U. S. Department of Agriculture, Washington, D. C.
ANDERSON, JOHN F.....U. S. Public Health and Marine-Hospital Service. Hygienic Laboratory, Washington, D. C.
ATKINSON, JAMES P.....Department of Health, New York City.
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OF THE

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EXPERIMENTAL BIOLOGY AND MEDICINE

SIXTY-FIRST MEETING

CORNELL UNIVERSITY MEDICAL COLLEGE

NEW YORK CITY

OCTOBER 21, 1914

AND

FIFTH MEETING

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OF THE

SOCIETY FOR

EXPERIMENTAL BIOLOGY AND MEDICINE

SIXTY-SECOND MEETING

NEW YORK POST-GRADUATE MEDICAL SCHOOL

NEW YORK CITY

NOVEMBER 18, 1914

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DECEMBER 16, 1914

AND

SIXTH MEETING

PACIFIC COAST BRANCH

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Members present at fifth meeting, Pacific Coast Branch:

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Dates of the next two regular meetings:

November 18, 1914.—December 16, 1914.

PROCEEDINGS

OF THE

SOCIETY FOR

EXPERIMENTAL BIOLOGY AND MEDICINE

SIXTY-FOURTH MEETING

COLLEGE OF PHYSICIANS AND SURGEONS

NEW YORK CITY

JANUARY 20, 1915

VOLUME XII

No. 4

NEW YORK

1915

CONTENTS.

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SOCIETY FOR

EXPERIMENTAL BIOLOGY AND MEDICINE

SIXTY-FIFTH MEETING

COLLEGE OF THE CITY OF NEW YORK

NEW YORK CITY

FEBRUARY 17, 1915

AND

SEVENTH MEETING
PACIFIC COAST BRANCH
SAN FRANCISCO, CALIFORNIA
FEBRUARY 3, 1915

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PATHOLOGICAL LABORATORY

BELLEVUE HOSPITAL

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Dates of the next two meetings:

March 17, 1915–April 21, 1915.

PROCEEDINGS

OF THE

SOCIETY FOR

EXPERIMENTAL BIOLOGY AND MEDICINE

SIXTY-SEVENTH MEETING

UNIVERSITY AND BELLEVUE HOSPITAL

MEDICAL COLLEGE

NEW YORK CITY

APRIL 21, 1915

AND

NINTH MEETING
PACIFIC COAST BRANCH
SAN FRANCISCO, CALIFORNIA
APRIL 7, 1915

VOLUME XII

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OF THE

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EXPERIMENTAL BIOLOGY AND MEDICINE

SIXTY-EIGHTH MEETING

ZOOLOGICAL DEPARTMENT

SCHERMERHORN HALL

COLUMBIA UNIVERSITY

NEW YORK CITY

MAY 19, 1915

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Dates of the next two meetings:

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Dates of the next two meetings:

October 20, 1915–November 17, 1915.